IN THE UNITED STATES DISTRICT COURT

FOR THE SOUTHERN DISTRICT OF FLORIDA

Case No. 15-cv-61631-JIC/BSS

AMGEN INC. and AMGEN MANUFACTURING LIMITED,

Plaintiffs,

vs.

APOTEX INC. and APOTEX CORP.,

Defendants.

REPLY MEMORANDUM OF LAW IN FURTHER SUPPORT OF PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION

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PRELIMINARY STATEMENT

The Federal Circuit's decision in *Amgen, Inc.* v. *Sandoz, Inc.*, 794 F.3d 1347 (Fed. Cir. 2015) is controlling precedent on the interpretation of 42 U.S.C. § 262(*l*) and the specific provision at issue here, paragraph (*l*)(8)(A). Considering that provision in the context of the entire, complex BPCIA, the Federal Circuit interpreted paragraph (*l*)(8)(A) simply and clearly: an Applicant must give 180 days' notice before first commercial marketing of its biosimilar product, and may give that notice only after FDA approval. Apotex seeks to avoid this controlling precedent by focusing on one sentence and a handful of additional words, by ignoring the rest of the majority's opinion, and by asking this Court to follow not the binding precedent but the dissent's view of the law. If Apotex wants to see *Amgen* overturned, its relief lies elsewhere (if anywhere). The majority's holding controls here, and Apotex must give notice.

First, Apotex argues that paragraph (*l*)(8)(A) is not a "mandatory," "standalone" provision (Apotex Br. at 1), but rather is mandatory only if the Applicant fails to provide its aBLA and manufacturing information under paragraph (*l*)(2)(A). The Federal Circuit squarely rejected this. It held that paragraph (*l*)(8)(A) is mandatory: "A question exists, however, concerning whether the 'shall' provision in paragraph (*l*)(8)(A) is mandatory. We conclude that it is." *Amgen*, 794 F.3d at 1359 (emphasis added). Tellingly, Apotex does not quote, or even cite, this language. The Federal Circuit further held that paragraph (*l*)(8)(A) is not tied to other provisions of subsection 262(*l*), but stands alone: "Paragraph (*l*)(8)(A) is a standalone notice provision in subsection (*l*) . . . ." *Id.* Apotex does not quote or cite this language either.

Instead, Apotex attempts to manufacture uncertainty by seizing on the phrasing of the following sentence at the conclusion of the majority's discussion of paragraph (*l*)(8)(A): "We therefore conclude that, where, as here, a subsection (k) applicant completely fails to provide its aBLA and the required manufacturing information to the RPS by the statutory deadline, the requirement of paragraph (*l*)(8)(A) is mandatory." *Id.* at 1360. Apotex reads this to imply the converse, namely that paragraph (*l*)(8)(A) is not mandatory if an Applicant provides its aBLA to the RPS, as Apotex did. But the statute does not condition notice under paragraph (*l*)(8)(A) on non-compliance with paragraph (*l*)(2)(A), and the Federal Circuit expressly stated that "nothing in paragraph (*l*)(8)(A) conditions the notice requirement on paragraph (*l*)(2)(A) or other provisions of subsection (*l*)." *Id.* Again, Apotex does not cite this language.

The sentence that Apotex quotes exists not to benefit Apotex but to condemn Sandoz. One of Sandoz's arguments was that it was excused from all of the provisions of subsection 262(*l*), including paragraph (*l*)(8)(A), because it "opted out" of the statute by refusing to provide its aBLA and manufacturing information. Judge Chen agreed with that, in dissent. *Id.* at 1367, 1369 (Chen, J., dissenting in part). The majority—having previously held that paragraph (*l*)(8)(A) is a "standalone notice provision" that is "mandatory"—confirmed that paragraph (*l*)(8)(A) is mandatory even for a truculent Applicant like Sandoz that "completely fails" at its disclosure obligations. That does not mean, however, that complying with paragraphs (*l*)(2) through (*l*)(4) excused Apotex from the standalone, mandatory provision of paragraph (*l*)(8)(A). The Federal Circuit majority held that paragraph (*l*)(8)(A) is mandatory for every Applicant, including Apotex. That holding controls here.

Second, Apotex argues that affording Amgen the 180 days' notice of paragraph (*l*)(8)(A) would be unfair because it would convert a mere "notice provision" into 180 days of marketing exclusivity for Amgen. (Apotex Br. at 1.) That was Sandoz's argument, too, *see id.* at 1358, and was a key part of Judge Chen's dissenting opinion, *see Amgen*, 794 F.3d at 1367 (Chen, J., dissenting in part). But the majority opinion rejected this argument, and held that while the 180-day notice provision may indeed follow the 12 years of statutory exclusivity, that is no reason to disregard the plain language of the statute:

> It is true that in this case . . . Amgen will have an additional 180 days of market exclusion after Sandoz's effective notice date; that is because Sandoz only filed its aBLA 23 years after Amgen obtained FDA approval of its Neupogen product. Amgen had more than an "extra" 180 days, but that is apparently the way the law, business, and the science evolved.

Id. at 1358 (majority opinion). The 180-day notice provision "provides 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." *Id.* Apotex repeatedly asserts that Amgen does not need such a window because it has no additional patents on which to seek a preliminary injunction. But the statute, the Federal Circuit instructs, must be interpreted not with respect to the "particular" facts of "a given case," but instead "as it is enacted," *id.*, which includes a 180-day period after FDA approval and before first commercial marketing. Apotex's further assertion that Amgen will not acquire any new patent rights on which a preliminary injunction could be sought during the notice period—as contemplated by paragraph (*l*)(7)—is pure speculation.

Third, Apotex argues that the BPCIA affords no means by which the Court can compel Apotex to comply with paragraph (*l*)(8)(A). And yet the means existed for the Federal Circuit to grant injunctive relief in *Amgen*. After holding that notice under paragraph (*l*)(8)(A) is mandatory and reversing the district court's "conclusion relating to its interpretation of § 262(*l*)(8)(A) and the date when Sandoz may market its product," *id.*, the majority forbade Sandoz from marketing its biosimilar product until 180 days after the day of notice of first commercial marketing. "Sandoz . . . may not market Zarxio before 180 days from March 6, 2015, *i.e.*, September 2, 2015," *id.* at 1360. Amgen seeks no more here.

ARGUMENT

I. The BPCIA Requires 180 Days' Notice of Commercial Marketing After Approval

The central issue before this Court is whether the 180-day notice provision in paragraph (*l*)(8)(A) is mandatory for all Applicants. The Federal Circuit held that it is.

A. The BPCIA and the *Amgen* Decision Make Clear That Notice Is Mandatory

The Court's analysis in a statutory construction case must "begin with the language of the statute." *Momenta Pharm., Inc.* v. *Amphastar Pharm., Inc.*, 686 F.3d 1348, 1353-54 (Fed. Cir. 2012). That makes it all the more striking that Apotex never quotes paragraph (*l*)(8)(A). The statute is clear: "The 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) (emphasis added).

Amgen cited Supreme Court and Federal Circuit cases holding that "shall" is ordinarily mandatory language. (Amgen Br. at 13-14.) Apotex does not distinguish these cases. Instead it says the Federal Circuit majority's discussion of the "shall" in a different provision, paragraph (*l*)(2)(A), is "instructive in this case." (Apotex Br. at 9.) It is, but it supports Amgen. The majority held that the "shall" in paragraph (*l*)(2)(A) appears mandatory, but that when read in the context of other provisions of subsection (*l*) and of the Patent Act, it is not mandatory. *Amgen*, 794 F.3d at 1355-56. But it then reached the opposite conclusion with respect to the "shall" in paragraph (*l*)(8)(A), the provision at issue on this motion: "A question exists, however, concerning whether the 'shall' provision in paragraph (*l*)(8)(A) is mandatory. We conclude that it is." *Id.* at 1359. The majority did not overlook the inconsistency in its constructions of "shall" in paragraphs (*l*)(2)(A) and (*l*)(8)(A); it spent nearly a full page explaining why paragraph (*l*)(8)(A) is mandatory even though it had concluded paragraph (*l*)(2)(A) is not. *Id.*

Judge Chen's dissent was critical of this part of the majority opinion, and Apotex quotes at length from that dissent. (Apotex Br. at 10.) But what matters here is not whether Apotex thinks that Judge Chen had the better argument. What matters is the controlling holding of the majority opinion that notice under paragraph (*l*)(8)(A) is mandatory. Apotex shall give that notice after FDA approval, and cannot begin marketing its product for 180 days thereafter.

B. The Majority's Holding Does Not Excuse Apotex From Giving Notice

Apotex's argument depends on the majority opinion's concluding sentence that "We therefore conclude that, where, as here, a subsection (k) applicant completely fails to provide its aBLA and the required manufacturing information . . . the requirement of paragraph (*l*)(8)(A) is mandatory." *Amgen*, 794 F.3d at 1360. Apotex argues that the majority meant to signal or "suggest" that only a fully recalcitrant Applicant like Sandoz must follow the mandate of paragraph (*l*)(8)(A). Apotex misunderstands. Sandoz attempted to frame all of subsection 262(*l*) as an option, and argued that an Applicant that elects not to provide its aBLA is excused from the rest of that subsection—a view with which Judge Chen agreed in dissent. *Id.* at 1367, 1369 (Chen, J., dissenting in part). After stating the purposes of paragraph (*l*)(8)(A) notice, however, the majority made clear that notice is mandatory for to all Applicants, even those—like Sandoz—who do not comply with paragraph (*l*)(2)(A). The majority did not, however, hold, state, or even imply (as Apotex would have it) the converse proposition, that an Applicant that does provide its aBLA is exempt from giving notice under paragraph (*l*)(8)(A).

Indeed, the majority opinion disavows the converse proposition. It says that "the 'shall' provision in paragraph (*l*)(8)(A) is mandatory." *Id.* at 1359 (majority opinion). That sentence contains no exceptions. It says that paragraph (*l*)(8)(A) is a "standalone" provision, meaning that its obligation exists separately of any other obligation. *Id.* And it says that "nothing in paragraph (*l*)(8)(A) conditions the notice requirement on paragraph (*l*)(2)(A) or other provisions of subsection (*l*)." *Id.* at 1360. And while that is sufficient to defeat Apotex's argument, there is even more: This part of Judge Lourie's opinion is the majority opinion because Judge Newman joined in it. Judge Newman's own opinion states, "I agree with the court that the notice of issuance of the FDA license is mandatory, and that this notice starts the 180-day stay of commercial marketing, in accordance with 42 U.S.C. § 262(*l*)(8)(A)." *Id.* at 1362 (Newman, J., dissenting in part). If Apotex were correct, and Judge Lourie's discussion of the mandatory nature of paragraph (*l*)(8)(A) applied to only Applicants like Sandoz that refuse to provide their

aBLA, then Judge Newman would not have joined this aspect of the opinion. It is the binding opinion of the court precisely because both Judge Newman and Judge Lourie held that paragraph (*l*)(8)(A) is mandatory for all Applicants.

Notably, Apotex never attempts to explain why an Applicant that provides its aBLA should then be excused from providing notice of commercial marketing. There is no logical connection between the two, and Apotex proffers none. Its argument is based purely on a misreading of the majority's opinion.

C. Paragraph (*l*)(9)(B) Does Not Permit Apotex to Refuse to Provide Notice Under Paragraph (*l*)(8)(A)

Apotex also focuses at length on the middle of a sentence in the majority opinion, in which the court wrote "paragraph (*l*)(9)(B) specifies the consequence for a subsequent failure to comply with paragraph (*l*)(8)(A) after the applicant has complied with paragraph (*l*)(2)(A) . . ." *Id.* at 1359 (majority opinion). Apotex reads this out of context to suggest that Amgen's only remedy for Apotex's repudiation of its notice obligation is to file a declaratory-judgment action under paragraph (*l*)(9)(B) and seek a patent-based preliminary injunction. Apotex places far more weight on that sentence fragment than it can bear.

Some context is helpful: In interpreting a different BPCIA provision, subsection 262(*l*)(2), the court found that paragraph (*l*)(9)(C) specifies the consequence for an Applicant's failure to comply with its paragraph (*l*)(2)(A) disclosure obligations. The court stated that where an Applicant "fails to provide the application and information required under paragraph (2)(A)," the RPS may bring an action for patent infringement under 42 U.S.C. § 262(*l*)(9)(C) and 35 U.S.C. § 271(e)(2)(C)(ii) and "access the required information through discovery." *Id.* at 1356. The court observed that treating the "shall" in paragraph (*l*)(2)(A) as mandating compliance in all circumstances would render these provisions of the Patent Act and subsection (*l*) "superfluous." *Id.* Importantly, the court also noted that the BPCIA violation triggering a paragraph (*l*)(9)(C) declaratory judgment—i.e., submitting an aBLA under subsection (k) but failing to provide paragraph (*l*)(2)(A) disclosures—was "precisely" an act of infringement under 35 U.S.C. § 271(e)(2)(C)(ii), for which another section of the Patent Act, 35 U.S.C. § 271(e)(4) limits available remedies. *Id.* Accordingly, the court concluded that the "only" consequences for a paragraph (*l*)(2)(A) violation are those available under 35 U.S.C. § 271(e)(4). *Id.* at 1357.

There is no parallel here. No provision in the Patent Act ties patent infringement to a failure to provide paragraph (*l*)(8)(A) notice or expressly limits available remedies for a failure to

provide that notice. And when it came to interpreting paragraph (*l*)(8)(A), the majority concluded that the declaratory-judgment provisions of paragraph (*l*)(9) did not suffice to make the "shall" in paragraph (*l*)(8)(A) optional. *Id.* at 1359. The court considered paragraph (*l*)(9)(B), which is the declaratory-judgment provision that refers to a failure to give notice under paragraph (*l*)(8)(A), and found it noteworthy that it "does not apply in" all circumstances. *Id.* Indeed, it did not apply to Sandoz's failure to give notice, because Sandoz had also failed to provide its aBLA, on which paragraph (*l*)(9)(B) depends. *Id.* Immediately after discussing and rejecting paragraph (*l*)(9)(B) as a consequence for failure to give paragraph (*l*)(8)(A) notice, the majority stated "Paragraph (*l*)(8)(A) is a standalone notice provision" and that "nothing in paragraph (*l*)(8)(A) conditions the notice requirement on paragraph (*l*)(2)(A) or other provisions of subsection (*l*)." *Id.* at 1359-60.

To be clear, Judge Chen's dissent agrees with Apotex's argument on this point. (Apotex's Br. at 10-11.) But Judge Chen was outvoted, 2-1, and it is the majority's decision that controls here. It is thus not open to Apotex to argue that paragraph (*l*)(9)(B) permits Apotex to refuse to provide notice under paragraph (*l*)(8)(A), or that some supposed superfluousness of that provision would excuse Apotex from its notice obligations. The Federal Circuit rejected that argument. Amgen notes, however, that Apotex's argument would be wrong if advanced on a clean slate. Paragraph (*l*)(9)(B) is not a remedial provision. It simply lifts a prohibition on declaratory judgments imposed by paragraph (*l*)(9)(A), which is why all of (*l*)(9) is entitled "Limitations on Declaratory Judgment." Paragraph (*l*)(9)(B) does not say the RPS must bring, or shall bring, a declaratory judgment, it says the RPS "may" do so. Nothing about that provision proposes to be a remedy, or an exclusive remedy, for failure to give paragraph (*l*)(8)(A) notice.

And if Apotex were right, and an Applicant could "elect" not to give 180 days' notice of commercial marketing, three things would be indisputably true:

- No Applicant would give notice. Applicants would have complete control over when to launch, rather than the courts having the ability to issue a timely preliminary injunction where warranted, and the balance Congress created between protecting innovators and biosimilar applicants would be destroyed.

- Faced with the exigent launch of a biosimilar competitor and the ensuing irreparable harm, the RPS would not seek a declaratory judgment; it would run to court with a

temporary restraining order and would sue for outright patent infringement under whichever portions of the Patent Act applied, including 35 U.S.C. § 271(a), (b), (c), or (g).

- The ensuing chaotic motion practice would rob the RPS, the court, and the public of the "defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product," *Amgen*, 794 F.3d at 1358, which, the Federal Circuit held, is the purpose of paragraph (*l*)(8)(A).

The Federal Circuit fully considered the argument that Apotex is now making, because Sandoz made it too. And a majority of that court, fully cognizant of paragraph (*l*)(9)(B), held that notice under paragraph (*l*)(8)(A) is mandatory and that refusal to provide that notice is remediable by an injunction prohibiting non-compliance. That holding is controlling here.

D. Notice Does Not Turn on Whether There Are Paragraph (*l*)(8)(B) Patents

Apotex argues that notice under paragraph (*l*)(8)(A) is not required here because the purpose of that provision is to allow the RPS to seek a preliminary injunction on the paragraph (*l*)(8)(B) patents and, Apotex says, Amgen has no such patents. (*See* Apotex Br, at 3, 7, 11–13.)

This misunderstands the purpose of the notice. Paragraph (*l*)(8)(A) affords the RPS not only the time to seek a preliminary injunction on existing patents, but also the ability to seek a preliminary injunction on patents that first issue or that the RPS first licenses after the RPS provides its initial patent list under paragraph (*l*)(3)(A). *See* 42 U.S.C. § 262(*l*)(7). The Federal Circuit held this too: Notice of commercial marketing "allows the RPS a period of time to seek a preliminary injunction based on patents that the parties initially identified during information exchange but were not selected for the immediate infringement action, as well as any newly issued or licensed patents." *Amgen*, 794 F.3d at 1352 (emphasis added). That is a very real possibility: the companies that are reference product sponsors under the BPCIA are often innovators, with expanding patent portfolios.

Apotex has no basis to conclude that Amgen will not obtain new, relevant patents before Apotex's 180-day notice period ends. In this regard, it is worth noting that Amgen does not know when or if FDA will approve Apotex's application. Apotex filed its aBLA on or about October 16, 2014. (Answer ¶ 25.) The FDA has set a goal of reviewing 70% of 2014 biosimilar filings within 10 months, and for Apotex that date—known as a "BsUFA date" because it comes from the Biosimilar User Fee Act of 2012—passed on or about August 15, 2015 with no action

by FDA.[1] The status of Apotex's application is a secret; it could have received a complete response from FDA noting major or minor deficiencies that could delay approval by many months, or it could have received no response at all. Apotex is a privately held company, and does not have the disclosure obligations of a public company. Thus, Amgen has no way to know now when the 180-day notice period will start or end, or to assess what patents it may have obtained, what patents may by then have expired, or how other facts may develop that would inform the propriety of seeking preliminary injunctive relief. And Apotex does not contest that Amgen will be irreparably harmed by not having the 180-day statutory period in which to make that assessment: Apotex stipulated that Amgen would be irreparably harmed if Apotex were to commence commercial marketing without providing notice "at least 180 days prior to commencing such commercial marketing." [D.E. 42-8 at 3.]

And in any event, Apotex cannot avoid the requirement of a statute by the specifics of this particular case. As the Federal Circuit held, "A statute must be interpreted as it is enacted, not especially in light of particular, untypical facts of a given case." *Amgen*, 794 F.3d at 1358. Even if Apotex were right that Amgen had no additional patents on which to seek a preliminary injunction, that would not excuse Apotex from complying with a statute that, on its face, requires Apotex to provide 180 days' notice of commercial marketing without qualification or exceptions.

II. The 180-Day Notice Provision Does Not Afford Improper Market Exclusivity

Apotex also argues that requiring an Applicant to give 180 days' notice would give Amgen an inappropriate additional 180 days of market exclusivity. Here, too, Apotex rehashes an argument the Federal Circuit rejected. Sandoz made this exact argument. Judge Chen agreed with it, in dissent. *Id.* at 1367 (Chen, J., dissenting in part). The majority recognized that Amgen would get in that case (and would get here) 180 days of "market exclusion." But it held, in precedent binding on this Court, that this consequence of the BPCIA is simply how the law works:

> It is true that in this case, as we decide *infra*, Amgen will have an additional 180 days of market exclusion after Sandoz's effective notice date; that is because Sandoz only filed its aBLA 23 years after Amgen obtained FDA approval of its Neupogen product. Amgen had more than an "extra" 180 days, but that is apparently the way the law, business, and the science evolved.

[1] *See* *http://www.fda.gov/downloads/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/UCM321015.pdf*. FDA's goal of reviewing 70% of 2014 filings in 10 months is on slide 11.

Id. at 1358 (majority opinion). Amgen argued that the 180-day period is not a period of exclusivity. There is nothing, for example, that prohibits one biosimilar version of a product from being on the market while a second biosimilar waits the 180-day period to launch. But the problem with Apotex's argument is not only that it is wrong, but that it is rejected by precedent.

III. The Court Has the Power to Compel Apotex to Comply with the Law

Apotex argues that this Court cannot compel Apotex to comply with paragraph (*l*)(8)(A). But its arguments are again foreclosed by the Federal Circuit's decision in *Amgen*. The core of Apotex's argument is that even if paragraph (*l*)(8)(A) "creates a right" to 180 days' post-approval notice before commercial marketing, paragraph (*l*)(9)(B) is the express and exclusive "remedy for violation of that right." (Apotex Br. at 13.) That is exactly the argument that the majority rejected in *Amgen*, holding that despite the existence of paragraph (*l*)(9)(B), the notice requirement in paragraph (*l*)(8)(A) is a "mandatory," "standalone notice provision." *Amgen*, 794 F.3d at 1359. And the Federal Circuit continued its injunction pending appeal until September 2, 2015, precisely 180 days after the notice that Sandoz provided to Amgen on the day of FDA approval. *Id.* at 1360–62. It did so "[i]n light of what we have decided concerning the proper interpretation of the contested provisions of the BPCIA," *id.* at 1362, including paragraphs (*l*)(8)(A) and (*l*)(9)(B). Apotex makes the curious argument that there is no right to injunctive relief "especially when the parties have followed the statutory framework" (Apotex Br. at 13), but that proves too much: Apotex is now proposing not to follow the statutory framework, because it is has announced its refusal to provide notice under paragraph (*l*)(8)(A). The Federal Circuit had made clear that an Applicant can be enjoined from launching its product until it has given that notice and waited the required 180 days.

IV. Any Bond Should Be Nominal, and Apotex Has Not Met Its Burden

Finally, Apotex seeks "a substantial bond" to ensure that it is fully compensated should an injunction be reversed as error. (Apotex Br. at 14.) In its moving brief, Amgen cited case law holding that no bond is needed where the prevailing party has a high probability of success on the merits. Apotex does not disagree with the legal principle (nor could it), but responds that because Judge Chen dissented and because there has been only one case construing the BPCIA, Amgen cannot demonstrate a high probability of success. That misses an important point: there is also only one circuit court of appeals that can hear cases about "any Act of Congress relating to patents," 28 U.S.C. § 1295(a)(1), and it has already spoken. The Federal Circuit resolved all

of these issues in Amgen's favor, and then denied Sandoz's petition to rehear paragraph (*l*)(8)(A)-related issues en banc.

On the facts, Apotex submitted a declaration seeking a substantial bond. Amgen notes, however, that the declaration that Apotex submitted in support of its application falls far short of the evidence needed. Apotex has done no more than submit an affidavit from its own President of Global Specialty Pharma in which he (i) assumes that Apotex's product will penetrate the market spectacularly faster than any other relevant product has done (Lydeamore Decl. ¶ 10 [D.E. 54]), growing to an assumed percentage of the market within a year (*id.* ¶ 15) (ii) uses an assumed price for Apotex's own product (*id.* ¶ 13) even though Apotex must know what its own price will actually be, (iii) assumes Apotex's ability to meet demand (*id.*) without any evidence to support that assumption, (iv) and then calculates the bond based on Apotex's revenue, rather than its profits, and without providing any information about, for example, cost of goods or cost of sales (*id.* ¶ 16). If Amgen were required to bond any amount more than a nominal one, it should be tied to evidence, not conjecture, and it should be the profits Apotex would lose during the period of a bond, not the top-line revenue it would earn on products it would not actually sell. That is a pure windfall to Apotex. Moreover, Apotex's unsubstantiated projections are far rosier than the real-world experiences of biologic and biosimilar competitors. For example, public analyst reports calculate that over its first full year on the market, Teva's Granix® product (to which Mr. Lydeamore refers) had 13% of the net revenue in the United States market for filgrastim. (Groombridge Supp. Decl. ¶ 4 & Ex. A.) Apotex's projections are also far rosier than the predictions of public analysts, which predict, for example, that Apotex will price its product far lower than Mr. Lydeamore assumes, will gain only 7% of the market, and will generate far less revenue than Mr. Lydeamore assumes. (Groombridge Supp. Decl. ¶ 3.) As the party seeking security, Apotex bears the burden of showing "a rational basis for the amount of the proposed bond." *Cont'l Grp., Inc.* v. *KW Prop. Mgmt., LLC*, Case No. 09-60202, 2009 U.S. Dist. LEXIS 101448, at *19 (S.D. Fla. Oct. 30, 2009). It has failed to meet that burden.

CONCLUSION

Amgen respectfully requests that the Court enter a preliminary injunction as set forth in the proposed order that accompanied Amgen's Motion for a Preliminary Injunction and Incorporated Memorandum of Law.

Dated: November 20, 2015

By: */s/ John F. O'Sullivan*

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on November 20, 2015, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to counsel and that a true and correct copy was served via electronic mail on all counsel of parties of record.

By: */s/ John F. O'Sullivan*____

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IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA

AMGEN INC. and AMGEN MANUFACTURING LIMITED, Plaintiff, v. APOTEX INC. and APOTEX CORP., Defendant.	Case No. 0:15-CV-61631-JIC/BSS

SUPPLEMENTAL DECLARATION OF NICHOLAS GROOMBRIDGE
IN FURTHER SUPPORT OF
AMGEN'S MOTION FOR A PRELIMINARY INJUNCTION

I, Nicholas Groombridge, declare and state as follows:

1. I am a member of the law firm of Paul, Weiss, Rifkind, Wharton & Garrison LLP, counsel for Plaintiffs Amgen Inc. and Amgen Manufacturing Limited (together, "Amgen") in this action. I make this declaration to place before the Court certain documents in further support of Amgen's motion for a preliminary injunction.

2. Through a declaration by Steven Lydeamore, Apotex has provided the Court with an estimate of its sales volume and revenue for the first six months following the launch of its biosimilar pegfilgrastim product.

3. Analysts have published estimates of the market penetration and revenue of biosimilar manufacturers like Apotex. The BioTrends Research Group released an Excel document entitled "Biosimilars Advisory Service: Market Forecast Assumptions for G-CSFs and MAbs in Oncology." I attach a copy of that Excel document here as Exhibit A. I note for the Court's convenience that the term "G-CSF" in the title refers to granulocyte colony stimulating factor, and that—as the parties here agree—Amgen's NEULASTA® is a G-CSF product.

(Complaint [Docket Entry No. 001] at ¶ 38; *accord* Answer [Docket Entry No. 035] at ¶ 38.) In the "NEULASTA" worksheet within Exhibit A, BioTrends forecasted that in all of 2016 in the United States, sales of biosimilar pegfilgrastim products—including not only Apotex's product, if approved, but also any other biosimilar products sold for therapeutic use in the United States during that period—will account for 7% of the total forecasted United States pegfilgrastim net revenue, which includes adjustments for discounts and rebates to customers. BioTrends further forecasted that the sales price for biosimilar pegfilgrastim would be 75% of the innovators' net price, and that biosimilar pegfilgrastim would be sold to 9% of the patients receiving pegfilgrastim products, for a total biosimilar pegfilgrastim net revenue of $249,000,000. Those data can be found in cells E11, E12, E15, and E 16 of the "NEULASTA" worksheet.

4. Mr. Lydeamore refers to a product named "Granix," from Teva Pharmaceuticals, Inc. Teva launched Granix in the United States market in approximately November, 2013. I attach as Exhibit B a copy of Teva's announcement of the launch of Granix, also available at http://ir.tevapharm.com/phoenix.zhtml?c=73925&p=irol-newsArticle_pf&ID=1877729. According to the BioTrends data, over the course of 2014, Granix's first full year on the market, Granix's share of the net revenue in the United States filgrastim market was 13%. That datum can be found in cell C25 of the "NEUPOGEN_GRAN" worksheet in Exhibit A.

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

Executed the 20 day of November, 2015, at New York, New York.

Nicholas Groombridge

EXHIBIT A

BioTrends RESEARCH GROUP
A Decision Resources Group Company

Biosimilars Advisory Service 2015

Senior Director: Kate Keeping **Principal Analyst: Anees Malik**
questions@teamdrg.com

Brand and Biosimilar Market Forecast and Assumptions: Neulasta / G-Lasta, 2014-2024 (millions of US dollars)

United States	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Baseline forecast (w/o biosimilars)	$ 3,649	$ 3,710	$ 3,750	$ 3,770	$ 3,781	$ 3,787	$ 3,790	$ 3,791	$ 3,792	$ 3,793	$ 3,793
Brand price adjustment	100%	100%	100%	92%	84%	80%	79%	78%	78%	78%	78%
Biosimilar price (% of brand)			75%	69%	62%	58%	57%	56%	56%	55%	55%
Biosimilar patient share			9%	23%	45%	65%	78%	85%	87%	87%	87%
Brand sales	**$ 3,649**	**$ 3,710**	**$ 3,418**	**$ 2,669**	**$ 1,736**	**$ 1,050**	**$ 642**	**$ 457**	**$ 394**	**$ 378**	**$ 375**
% market share	100%	100%	93%	82%	62%	42%	27%	20%	18%	17%	17%
Biosimilar sales	**$ -**	**$ -**	**$ 249**	**$ 601**	**$ 1,048**	**$ 1,445**	**$ 1,695**	**$ 1,802**	**$ 1,828**	**$ 1,823**	**$ 1,808**
% market share	0%	0%	7%	18%	38%	58%	73%	80%	82%	83%	83%
Total market	**$ 3,649**	**$ 3,710**	**$ 3,667**	**$ 3,270**	**$ 2,784**	**$ 2,495**	**$ 2,337**	**$ 2,259**	**$ 2,222**	**$ 2,201**	**$ 2,183**

EU5 (France, Germany, Italy, Spain, UK)	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Baseline forecast (w/o biosimilars)	$ 549	$ 527	$ 487	$ 470	$ 469	$ 469	$ 469	$ 468	$ 468	$ 468	$ 468
Brand price adjustment	100%	100%	100%	100%	83%	75%	72%	70%	70%	70%	70%
Biosimilar price (% of brand)				70%	58%	52%	50%	49%	49%	49%	49%
Biosimilar patient share				8%	20%	39%	59%	73%	81%	84%	85%
Brand sales	**$ 549**	**$ 527**	**$ 487**	**$ 430**	**$ 313**	**$ 213**	**$ 139**	**$ 90**	**$ 64**	**$ 53**	**$ 49**
% market share	100%	100%	100%	94%	85%	69%	50%	35%	26%	22%	20%
Biosimilar sales	**$ -**	**$ -**	**$ -**	**$ 28**	**$ 54**	**$ 96**	**$ 138**	**$ 168**	**$ 185**	**$ 192**	**$ 195**
% market share	0%	0%	0%	6%	15%	31%	50%	65%	74%	78%	80%
Total market	**$ 549**	**$ 527**	**$ 487**	**$ 458**	**$ 367**	**$ 309**	**$ 277**	**$ 258**	**$ 249**	**$ 245**	**$ 244**

Japan	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Baseline forecast (w/o biosimilars)	$ 3	$ 68	$ 113	$ 143	$ 172	$ 195	$ 213	$ 228	$ 237	$ 243	$ 248
Brand price adjustment	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Biosimilar price (% of brand)											
Biosimilar patient share											
Brand sales	**$ 3**	**$ 68**	**$ 113**	**$ 143**	**$ 172**	**$ 195**	**$ 213**	**$ 228**	**$ 237**	**$ 243**	**$ 248**
% market share				100%	100%	100%	100%	100%	100%	100%	100%
Biosimilar sales	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**	**$ -**
% market share				0%	0%	0%	0%	0%	0%	0%	0%
Total market	**$ 3**	**$ 68**	**$ 113**	**$ 143**	**$ 172**	**$ 195**	**$ 213**	**$ 228**	**$ 237**	**$ 243**	**$ 248**

7 Major Markets Total	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Baseline forecast (w/o biosimilars)	$ 4,201	$ 4,304	$ 4,351	$ 4,383	$ 4,422	$ 4,451	$ 4,471	$ 4,488	$ 4,497	$ 4,504	$ 4,509
Brand sales	**$ 4,201**	**$ 4,304**	**$ 4,019**	**$ 3,242**	**$ 2,221**	**$ 1,458**	**$ 994**	**$ 775**	**$ 695**	**$ 674**	**$ 672**
% market share	100%	100%	94%	84%	67%	49%	35%	28%	26%	25%	25%
Biosimilar sales	**$ -**	**$ -**	**$ 249**	**$ 629**	**$ 1,102**	**$ 1,541**	**$ 1,833**	**$ 1,970**	**$ 2,013**	**$ 2,015**	**$ 2,003**
% market share	0%	0%	6%	16%	33%	51%	65%	72%	74%	75%	75%

NEULASTA

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
47		**Total market**	**$ 4,201**	**$ 4,304**	**$ 4,268**	**$ 3,871**	**$ 3,323**	**$ 2,999**	**$ 2,827**	**$ 2,745**	**$ 2,708**	**$ 2,689**	**$ 2,675**	
48														
49													Source: BioTrends Research Group	
50		Note: All baseline forecasts as of April 2015. Sales in 2014 are based on company-reported net revenue												
51														
52														
53														

BioTrends RESEARCH GROUP
A Decision Resources Group Company

Biosimilars Advisory Service 2015

Senior Director: Kate Keeping **Principal Analyst: Anees Malik**
questions@teamdrg.com

Brand and Biosimilar Market Forecast and Assumptions: Neupogen / Gran, 2014-2024 (millions of US dollars)

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
United States											
Baseline Neupogen forecast (w/o biosimilars)	$ 839	$ 746	$ 618	$ 504	$ 489	$ 439	$ 432	$ 426	$ 420	$ 417	$ 416
Neupogen price adjustment	100%	100%	83%	75%	72%	70%	70%	70%	70%	70%	70%
Baseline Granix forecast (w/o biosimilars)	$ 125	$ 190	$ 280	$ 360	$ 390	$ 405	$ 410	$ 414	$ 417	$ 418	$ 419
Granix price adjustment	100%	100%	83%	74%	70%	68%	68%	67%	67%	66%	66%
Biosimilars price (% of Neupogen)		80%	66%	59%	56%	55%	54%	54%	53%	53%	53%
Biosimilars patient share from Neupogen		2%	7%	19%	35%	48%	57%	61%	62%	63%	63%
Biosimilars price (% of Granix)		100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Biosimilars patient share from Granix		2%	7%	19%	35%	48%	57%	61%	62%	63%	63%
Neupogen sales	**$ 839**	**$ 731**	**$ 479**	**$ 304**	**$ 228**	**$ 160**	**$ 131**	**$ 117**	**$ 111**	**$ 109**	**$ 109**
% reference brand market share	100%	98%	92%	74%	54%	39%	31%	28%	26%	26%	26%
% total filgrastim market share	87%	78%	65%	48%	38%	29%	24%	22%	21%	21%	21%
Biosimilar sales	**$ -**	**$ 16**	**$ 44**	**$ 109**	**$ 191**	**$ 250**	**$ 291**	**$ 308**	**$ 312**	**$ 311**	**$ 309**
% reference brand market share	0%	2%	8%	26%	46%	61%	69%	72%	74%	74%	74%
% total filgrastim market share	0%	2%	6%	17%	32%	45%	54%	58%	59%	59%	59%
Total reference brand and biosimilar market	**$ 839**	**$ 747**	**$ 523**	**$ 413**	**$ 419**	**$ 410**	**$ 422**	**$ 425**	**$ 423**	**$ 420**	**$ 418**
Granix sales	**$ 125**	**$ 186**	**$ 216**	**$ 214**	**$ 178**	**$ 143**	**$ 120**	**$ 109**	**$ 105**	**$ 103**	**$ 103**
% market share (total filgrastim market)	13%	20%	29%	34%	30%	26%	22%	20%	20%	20%	20%
Total filgrastim market	**$ 964**	**$ 933**	**$ 739**	**$ 627**	**$ 597**	**$ 553**	**$ 542**	**$ 534**	**$ 528**	**$ 523**	**$ 521**
EU5 (France, Germany, Italy, Spain, UK)											
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Neupogen sales	$ 122	$ 117	$ 115	$ 112	$ 112	$ 111	$ 110	$ 109	$ 109	$ 109	$ 109
% filgrastim market share	35%	32%	31%	30%	29%	29%	29%	28%	28%	28%	28%
% short-acting G-CSF market share	24%	23%	23%	22%	22%	22%	22%	22%	22%	22%	22%
Biosimilar sales	$ 229	$ 244	$ 256	$ 264	$ 269	$ 272	$ 273	$ 275	$ 275	$ 276	$ 276
% filgrastim market share	65%	68%	69%	70%	71%	71%	71%	71%	72%	72%	72%
% short-acting G-CSF market share	46%	48%	50%	52%	53%	54%	55%	55%	56%	56%	56%
Total filgrastim market	**$ 350**	**$ 361**	**$ 371**	**$ 377**	**$ 381**	**$ 382**	**$ 383**	**$ 384**	**$ 384**	**$ 384**	**$ 384**
Granocyte (lenograstim) sales	**$ 147**	**$ 144**	**$ 137**	**$ 130**	**$ 125**	**$ 120**	**$ 116**	**$ 112**	**$ 110**	**$ 108**	**$ 107**
% market share	30%	29%	27%	26%	25%	24%	23%	23%	22%	22%	22%
Total short-acting G-CSF market	**$ 497**	**$ 505**	**$ 508**	**$ 507**	**$ 506**	**$ 502**	**$ 499**	**$ 496**	**$ 494**	**$ 492**	**$ 491**
Japan											
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Gran sales	$ 87	$ 56	$ 52	$ 44	$ 39	$ 37	$ 35	$ 36	$ 36	$ 36	$ 36
% filgrastim market share	86%	69%	59%	52%	47%	43%	41%	41%	41%	41%	40%
% short-acting G-CSF market share	56%	43%	39%	34%	31%	29%	28%	29%	29%	29%	29%
Biosimilar sales	$ 14	$ 26	$ 36	$ 41	$ 45	$ 48	$ 50	$ 51	$ 52	$ 52	$ 53
% filgrastim market share	14%	31%	41%	48%	54%	56%	59%	59%	59%	60%	59%
% short-acting G-CSF market share	9%	20%	27%	32%	36%	38%	41%	41%	42%	42%	42%

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
47		**Total filgrastim market**	**$ 101**	**$ 81**	**$ 88**	**$ 85**	**$ 84**	**$ 85**	**$ 84**	**$ 87**	**$ 88**	**$ 88**	**$ 89**	
48		**Neutrogin (lenograstim) sales**	**$ 55**	**$ 48**	**$ 46**	**$ 43**	**$ 42**	**$ 40**	**$ 39**	**$ 37**	**$ 37**	**$ 36**	**$ 36**	
49		% market share	35%	37%	34%	34%	33%	32%	32%	30%	29%	29%	29%	
50		**Total short-acting G-CSF market**	**$ 156**	**$ 129**	**$ 134**	**$ 128**	**$ 126**	**$ 125**	**$ 123**	**$ 124**	**$ 125**	**$ 124**	**$ 125**	
51		**7 Major Markets Total**												
52			**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	
53		**Reference brand sales**	**$ 1,047**	**$ 904**	**$ 646**	**$ 461**	**$ 379**	**$ 307**	**$ 275**	**$ 262**	**$ 256**	**$ 253**	**$ 253**	
54		% market share	74%	66%	54%	42%	36%	30%	27%	26%	26%	25%	25%	
55		**Biosimilar sales**	**$ 242**	**$ 286**	**$ 336**	**$ 414**	**$ 505**	**$ 570**	**$ 614**	**$ 634**	**$ 639**	**$ 639**	**$ 638**	
56		% market share	17%	21%	28%	38%	48%	56%	61%	63%	64%	64%	64%	
57		**Total reference brand and biosimilar market**	**$ 1,290**	**$ 1,190**	**$ 982**	**$ 875**	**$ 884**	**$ 877**	**$ 890**	**$ 896**	**$ 895**	**$ 893**	**$ 891**	
58		**Total filgrastim market**	**$ 1,415**	**$ 1,375**	**$ 1,198**	**$ 1,089**	**$ 1,062**	**$ 1,020**	**$ 1,009**	**$ 1,005**	**$ 1,000**	**$ 995**	**$ 994**	
59														
60														
61		Note: All baseline forecasts as of April 2015. Sales in 2014 are based on company-reported net revenue												
62														
63														

Source: BioTrends Research Group

EXHIBIT B

News Release

Teva Announces Updates to Oncology Biologic Portfolio

- First EU launch for LONQUEX® (long-acting G-CSF) in Germany; Teva launches GRANIX™ (short-acting G-CSF) launched in the US
- Balugrastim Biologics License Application (BLA) withdrawn from FDA review process pending provision of additional confirmatory data

JERUSALEM--(BUSINESS WIRE)--Nov. 18, 2013-- Teva Pharmaceutical Industries Ltd. (NYSE:TEVA) today announced two significant additions to its global oncology biologic portfolio with the recent launches of LONQUEX® (lipegfilgrastim) and GRANIX™ (tbo-filgrastim) Injection, and an update on the review status of balugrastim by the U.S. Food and Drug Administration (FDA).

Teva launched LONQUEX® (long-acting G-CSF) in Germany on November 4, 2013 – the first launch as part of an EU-wide approval. Teva plans to continue the roll-out of Lonquex across additional countries covered by the European Marketing Approval over the coming months. Also this month, Teva launched GRANIX™ (short-acting G-CSF) in the U.S. on November 11, 2013, marking the entry of the first new G-CSF to the US market in more than ten years. LONQUEX® and GRANIX™ provide new treatment options for physicians who are seeking to reduce the duration of severe neutropenia in patients with non-myeloid malignancies, who are receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

"Managing the duration of severe neutropenia is critical to optimal cancer care, because it can disrupt the delivery of cancer treatments," said Lee S. Schwartzberg, M.D., Division Chief, Hematology & Oncology, at the University of Tennessee Health Science Center. "With the availability of more G-CSF treatment options, healthcare professionals and their patients with non-myeloid malignancies undergoing myelosuppressive chemotherapy will be able to choose the G-CSF that best suits their needs."

"Teva is committed to commercializing G-CSFs globally and is continuing to build the portfolio of short- and long-acting G-CSFs in this important, patient-focused category of medicines," said Rob Koremans, M.D., President and CEO of Teva Global Specialty Medicines. "By making these treatment options available to physicians and their patients, our goal is to make a meaningful difference in the lives of those with cancer."

Last week, the company withdrew its balugrastim Biologics License Application (BLA) from the FDA review process following ongoing consultation with the agency in preparation for the late cycle review meeting, pending the provision of additional confirmatory data. The FDA has agreed to work with Teva in designing any additional studies that may be required in support of the BLA for balugrastim. The company is currently assessing its options with regard to its long-acting G-CSF program in order to define an approach that will best serve patient needs going forward.

About Neutropenia

Neutropenia is a hematological disorder characterized by an abnormally low number of neutrophils. A person with severe neutropenia has an absolute neutrophil count that is less than 500 mm^2 and has a high risk of infection. Neutrophils usually make up 40-60 percent of circulating white blood cells and serve as the primary defense against infections by destroying bacteria in the blood. When

chemotherapy agents attack cancer cells in the body, neutrophils and other cells are also attacked. This results in a decrease in healthy white blood cells, making it harder for the body to fight infections. Patients receiving chemotherapy are at risk of becoming neutropenic and can become susceptible to infections that may become life-threatening.

About G-CSF

G-CSF is a naturally occurring hormone that is produced by the body to stimulate the bone marrow to produce neutrophils, a type of white blood cell that helps the immune system fight infection. A recombinant form of G-CSF is used to treat certain cancer patients with neutropenia in order to stimulate the bone marrow to produce more white blood cells.

About Granix™

GRANIX™ is a leukocyte growth factor indicated for reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

The safety of GRANIX™ was evaluated in three Phase 3 clinical trials in patients receiving myelosuppressive chemotherapy for breast cancer, lung cancer, and non-Hodgkin lymphoma (NHL). In a Phase 3 clinical study, GRANIX™ demonstrated a 71 percent reduction in the duration of severe neutropenia when compared to placebo. GRANIX™ significantly reduced the duration of severe neutropenia when compared to placebo (1.1 days vs. 3.8 days). The efficacy of GRANIX was evaluated in a multinational, multicenter, randomized, controlled Phase 3 study of chemotherapy-naïve patients with high-risk stage II, stage III, or stage IV breast cancer receiving a myelosuppressive regimen of doxorubicin (60 mg/m^2 IV bolus) and docetaxel (75 mg/m^2). Comparisons with placebo occurred in the first cycle.

Important Safety Information

- **Splenic rupture:** Splenic rupture, including fatal cases, can occur following the administration of human granulocyte colony-stimulating factors (hG-CSFs). Discontinue GRANIX and evaluate for an enlarged spleen or splenic rupture in patients who report upper abdominal or shoulder pain after receiving GRANIX.
- **Acute respiratory distress syndrome (ARDS):** ARDS can occur in patients receiving hGCSFs. Evaluate patients who develop fever and lung infiltrates or respiratory distress after receiving GRANIX, for ARDS. Discontinue GRANIX in patients with ARDS.
- **Allergic reactions:** Serious allergic reactions, including anaphylaxis, can occur in patients receiving hG-CSFs. Reactions can occur on initial exposure. Permanently discontinue GRANIX in patients with serious allergic reactions. Do not administer GRANIX to patients with a history of serious allergic reactions to filgrastim or pegfilgrastim.
- **Use in patients with sickle cell disease:** Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving hG-CSFs. Consider the potential risks and benefits prior to the administration of GRANIX in patients with sickle cell disease. Discontinue GRANIX in patients undergoing a sickle cell crisis.
- **Potential for tumor growth stimulatory effects on malignant cells:** The granulocyte colony-stimulating factor (G-CSF) receptor, through which GRANIX acts, has been found on tumor cell lines. The possibility that GRANIX acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which GRANIX is not approved, cannot be excluded. [4]
- **Most common treatment-emergent adverse reaction:** The most common treatment-emergent adverse reaction that occurred in patients treated with GRANIX at the recommended dose with an incidence of at least 1% or greater and two times more frequent than in the placebo group was bone pain.

You are encouraged to report side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call 1-800-FDA-1088.

Please click **here** to view the Full Prescribing Information for GRANIX.

To view multimedia content for GRANIX™, please click:
www.TheGranixchoice.com

About Lonquex® (lipegfilgrastim)

Lonquex® is a new long-acting recombinant granulocyte colony-stimulating factor (G-CSF) treatment granted approval by the European Medicines Agency indicated for reduction in the duration and incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukemia and myelodysplastic syndromes).

Human G-CSF (filgrastim) is a polypeptide that regulates the production and release of functional neutrophils from the bone marrow. Lonquex® is a glycoPEGylated, long-acting form of recombinant human filgrastim, classified with a unique Anatomical Therapeutic Chemical (ATC) Classification System code, with a sustained duration of action due to decreased renal clearance.

The efficacy and tolerability of Lonquex® has been assessed in a full clinical development program. Phase I PK and PD studies in healthy volunteers demonstrate a marked increase in blood neutrophil counts within 24 hours of administration, as well as an increase in the antibacterial activities of neutrophils.

In a pivotal Phase III active-controlled study in 202 patients with stage II-IV breast cancer receiving up to four cycles of chemotherapy consisting of doxorubicin and docetaxel, patients were randomized 1:1 to receive 6 mg Lonquex® or 6 mg pegfilgrastim. The study met the primary efficacy endpoint, DSN in the first cycle of chemotherapy, demonstrating non-inferiority of 6 mg Lonquex® to 6 mg pegfilgrastim (p=0.126), with a comparable tolerability profile. (DSN was calculated as the sum of all days after CTX with ANC <0.5 x 10^9/L.) Secondary

endpoints were favorable for Lonquex®, including an overall mean faster time of 1.5 days to Absolute Neutrophil Count (ANC) recovery of in cycle 1, a trend that was maintained up to cycle 3 (ATP population). (ANC recovery defined as a return of ANC to ≥ $2.0x10^9$/L.)

A second Phase III study in 375 patients at low risk of febrile neutropenia (FN 10-20%) with non-small cell lung cancer was undertaken, comparing 6 mg Lonquex® (n=250) with placebo (n=125). The primary endpoint, incidence of FN in the first cycle of chemotherapy, did not reach statistical significance (p=0.1151). FN is defined as an ANC count of $<0.5\times10^9$/L with fever (oral body temperature >38.5ºC on ≥2 consecutive measurements ≥60 minutes apart.) Secondary endpoint analyses showed a positive trend in favor of Lonquex® vs placebo: duration and incidence of severe neutropenia in cycle 1 was consistently shorter (mean 2.3 ± 2.5 days; p<0.0001) and lower (32.1% vs 59.2%; p<0.0001) in the lipegfilgrastim group overall (mean 0.6 ± 1.1 days) compared with the placebo group. (SN defined as grade 4 neutropenia with an ANC $<0.5 \times 10^9$/L.) Although incidence of death at study end was 7.2 % (placebo) and 12.5 % (6 mg lipegfilgrastim), the overall incidence of death at the 360-day follow-up was similar between placebo and lipegfilgrastim (44.8 % and 44.0 %, respectively; safety population).

The tolerability of lipegfilgrastim has been evaluated based on results from clinical studies including 506 patients and 76 healthy volunteers treated at least once with lipegfilgrastim. The most common adverse reactions (≥ 1/100 to < 1/10) included: thrombocytopenia, hypokaleamia, headache, erythema and chest pain, with musculoskeletal pains listed as very common (≥ 1/10).

One 6 mg dose of Lonquex® (a single pre-filled syringe) is recommended for adults for each chemotherapy cycle, given approximately 24 hours after cytotoxic chemotherapy.

Lonquex® treatment should be initiated and supervised by physicians experienced in oncology or haematology. Please consult the SmPC for further information, including regarding adverse events, special warnings and precautions for use.

This medicinal product is subject to additional monitoring which will allow Teva to quickly identify new safety information. Healthcare professionals are encouraged to report any suspected adverse reactions to **PatientSafety@tevapharm.com**

About Balugrastim

Balugrastim is a once per cycle leukocyte growth factor. The proposed indication is to decrease the duration of severe neutropenia in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

About Teva

Teva Pharmaceutical Industries Ltd. (NYSE:TEVA) is a leading global pharmaceutical company, committed to increasing access to high-quality healthcare by developing, producing and marketing affordable generic drugs as well as innovative and specialty pharmaceuticals and active pharmaceutical ingredients. Headquartered in Israel, Teva is the world's leading generic drug maker, with a global product portfolio of more than 1,000 molecules and a direct presence in about 60 countries. Teva's branded businesses focus on CNS, oncology, pain, respiratory and women's health therapeutic areas as well as biologics. Teva currently employs approximately 46,000 people around the world and reached $20.3 billion in net revenues in 2012.

Teva's Safe Harbor Statement under the U. S. Private Securities Litigation Reform Act of 1995:

This release contains forward-looking statements, which express the current beliefs and expectations of management. Such statements

involve a number of known and unknown risks and uncertainties that could cause our future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to: our ability to develop and commercialize additional pharmaceutical products, including our ability to develop, manufacture, market and sell biopharmaceutical products, competition for our innovative medicines, especially Copaxone® (including competition from innovative orally-administered alternatives, as well as from potential purported generic equivalents), competition for our generic products (including from other pharmaceutical companies and as a result of increased governmental pricing pressures), competition for our specialty pharmaceutical businesses, our ability to achieve expected results through our specialty, including innovative, R&D efforts, the effectiveness of our patents and other protections for innovative products, decreasing opportunities to obtain U.S. market exclusivity for significant new generic products, our ability to identify, consummate and successfully integrate acquisitions and license products, our ability to reduce operating expenses to the extent and during the timeframe intended by our cost restructuring program, uncertainties relating to the replacement of and transition to a new President & Chief Executive Officer, the effects of increased leverage as a result of recent acquisitions, the extent to which any manufacturing or quality control problems damage our reputation for high quality production and require costly remediation, our potential exposure to product liability claims to the extent not covered by insurance, increased government scrutiny in both the U.S. and Europe of our settlement agreements with brand companies and liabilities arising from class action litigation and other third-party claims relating to such agreements, potential liability for sales of generic medicines prior to a final resolution of outstanding patent litigation, our exposure to currency fluctuations and restrictions as well as credit risks, the effects of reforms in healthcare regulation and pharmaceutical pricing and reimbursement, any failures to comply with complex Medicare and Medicaid reporting and payment

obligations, governmental investigations into sales and marketing practices ,particularly for our specialty medicines (and our ongoing FCPA investigations and related matters), uncertainties surrounding the legislative and regulatory pathways for the registration and approval of biotechnology-based medicines, adverse effects of political or economic instability, corruption, major hostilities or acts of terrorism on our significant worldwide operations, interruptions in our supply chain or problems with our information technology systems that adversely affect our complex manufacturing processes, any failure to retain key personnel or to attract additional executive and managerial talent, the impact of continuing consolidation of our distributors and customers, variations in patent laws that may adversely affect our ability to manufacture our products in the most efficient manner, potentially significant impairments of intangible assets and goodwill, potential increases in tax liabilities resulting from challenges to our intercompany arrangements, the termination or expiration of governmental programs or tax benefits, environmental risks, and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2012 and in our other filings with the U.S. Securities and Exchange Commission. Forward-looking statements speak only as of the date on which they are made and the Company undertakes no obligation to update or revise any forward looking statement, whether as a result of new information, future events or otherwise.

Source: Teva Pharmaceutical Industries Ltd.

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