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VIA FACSIMILE AND HAND DELIVERY

March 25, 2007

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Dear Mr. Bradshaw and Ms. Dickinson:

On behalf of Pfizer we are providing our views as to why the ANDA filed by Apotex for amlodipine besylate is not immediately approvable despite the ruling by the Federal Circuit on March 22, 2007, holding that Pfizer's '303 patent is invalid. It is Pfizer's view that Apotex' tentatively approved ANDA remains subject to Mylan's 180 day exclusivity until expiration of the patent and then subject to Pfizer's pediatric exclusivity at least until the issuance of the mandate by the Federal Circuit.

As you are aware, Apotex filed a Paragraph IV certification on June 23, 2003 and was timely sued by Pfizer. Pfizer received notification of this certification on July 7, 2003. Pfizer timely filed an action for patent infringement, triggering a 30-month stay that expired on January 7, 2006.

On January 29, 2006, the district court held that Pfizer's patent was valid and infringed and issued an order resetting Apotex' approval date to no earlier than the date of patent expiry, which is this Sunday, March 25, 2007. As such Apotex was subject both to Mylan's 180 day exclusivity as the first filer and would be additionally subject to Pfizer's pediatric exclusivity under the holding in *Mylan Labs. Inc. v. Thompson.* As explained further below, the March 22 ruling of the Federal Circuit does not change this because Apotex remains under the district court injunction at least until the mandate of the Federal Circuit issues.

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The Federal Circuit Decision Has No Immediate Effect On the District Court Judgment

Under the Federal Rules of Appellate Procedure, an appellate court opinion is effectuated through a mandate. "The mandate is effective when issued." F.R.A.P. 41(c). A mandate does not issue until disposition of a timely motion for rehearing.[1]

Because no mandate has yet issued, the Federal Circuit's ruling on March 22 has no effect on the district court's order enjoining approval of Apotex's ANDA. That order remains in effect, and should be respected by FDA. Indeed, FDA's traditional practice and its regulations support this approach. FDA guidance on ANDA approvals clearly states that, where a district court's decision upholding a patent in Paragraph IV litigation is reversed on appeal, the agency cannot approve the pending ANDA until "the date the district court issues a judgment that the patent is invalid, unenforceable, or not infringed *pursuant to a mandate issued by a court of appeals*." *See* FDA Guidance, *Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, ¶ IV.A (March 2000). FDA's regulations regarding ANDA approvals also recognize the importance of avoiding premature actions based on judgments that are not final. The regulations require an ANDA applicant to notify FDA of "a final judgment" in patent litigation, 21 C.F.R. § 314.107(e), and establish the ANDA's approval date based on "the date the court enters judgment." 21 C.F.R. § 314.107(b)(3)(ii).

If FDA were to approve Apotex's ANDA prior to issuance of the appeals court's mandate, that approval would essentially be in breach of a still-effective district court order. For FDA to act prior to issuance of the mandate would subvert the appellate processes—including rehearings—that are intended to enhance the correctness and finality of appellate rulings. This would be contrary to the purpose of Rule 41, which stays the mandate in order to maintain the status quo until post-judgment petitions are resolved.

Pfizer has 14 days following the March 22 ruling in which to seek rehearing. F.R.A.P. 40(a). Pfizer will file a petition for rehearing within that 14-day filing period,

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[1] Under Rule 41, the mandate "must issue 7 calendar days after the time to file a petition for rehearing expires, or 7 calendar days after entry of an order denying a timely petition for panel rehearing, petition for rehearing en banc, or motion for stay of mandate, whichever is later," although "[t]he court may shorten or extend the time." F.R.A.P. 41(b). Pfizer thus has 14 days following the Federal Circuit's entry of judgment to file a petition for rehearing en banc. F.R.A.P. 40(a). The mandate is automatically stayed upon timely filing of a petition for rehearing. F.R.A.P. 41(d)(1). If rehearing is granted, the mandate will not issue until the rehearing is resolved. If the petition for rehearing is denied, the mandate will issue within 7 days. F.R.A.P. 41(b). Thus the mandate is the mechanism for finalizing and effectuating an opinion of the court.

If Pfizer's the petition for rehearing in the Federal Circuit were to be denied, Pfizer would have 7 days to move to stay issuance of the mandate pending filing of a petition for certiorari to the U.S. Supreme Court. F.R.A.P. 41(d)(2). Timely filing of a motion for stay of mandate stays the mandate until disposition of the motion. For this motion to be granted, the petition would have to present a substantial question and there would have to be good cause for a stay. F.R.A.P. 41(d)(2)(A).

and is making every effort to do so as soon as possible. Thus, the mandate will not issue until Pfizer's petition is resolved, and the Federal Circuit's March 22 ruling will not take effect until that time. It would be inappropriate, and would undermine the appellate process, for FDA to take action on Apotex's ANDA before the rehearing process is resolved and the Federal Circuit's mandate issues.

Section 355(j)(5)(B)(iii)(II)(aa)(AA) Does Not Authorize FDA to Approve Apotex's ANDA Before a Mandate Issues

Section 355(j)(5)(B)(iii)(II)(aa)(AA) provides in relevant part that where a Paragraph IV certification is filed and the patent holder files suit within 45 days of receiving notice of that certification, the ANDA approval "shall be made effective upon the expiration of [the 30-month stay of ANDA approval] . . . except that if before the expiration of [the 30-month stay] the district court decides that the patent has been infringed," and if the district court judgment is appealed, the ANDA approval "shall be made effective on the date on which the court of appeals decides that the patent is invalid or not infringed." 21 U.S.C. § 355(j)(5)(B)(iii)(II)(aa)(AA). This provision is not applicable in this case, because it operates only "if before the expiration of [the 30-month stay] the district court decides that the patent has been infringed" (emphasis added). 21 U.S.C. § 355(j)(5)(B)(iii)(II); see also *Mylan Labs., Inc. v. Thompson*, 389 F.3d 1272, 1275 (D.C. Cir. 2004) (under section 355(j)(5)(B)(iii)(II)(aa)(AA), "[i]f the district court issues a ruling *during the 30-month stay period*, the ANDA approval date is determined by the decision of the district court, or the appellate court if appealed") (emphasis added). Here, the 30 month stay of Apotex's ANDA expired on January 7, 2006—prior to the district court decision on January 29, 2006. Thus, section 355(j)(5)(B)(iii)(II)(aa)(AA) does not apply here.

Even if section 355(j)(5)(B)(iii)(II)(aa)(AA) applied, it does not authorize FDA to approve Apotex's ANDA based on the non-final ruling the Federal Circuit issued on March 22. Consistent with the argument above, section 355(j)(5)(B)(iii)(II)(aa)(AA) should be applied in a manner that acknowledges and respects the processes for generating final appellate rulings.[2] If FDA were to approve Apotex's ANDA based on the opinion that issued Thursday, it would be undermining the legal processes for establishing the finality of the Federal Circuit's decision.

Pfizer notes as well that even once the Federal Circuit's mandate issues, Apotex' ANDA is not automatically approved. FDA must still review the ANDA before converting its current tentative approval to a final, effective approval. See *Mylan Labs. Inc. v. Thompson*, 332 F.Supp.2d 106, 124 (D. D.C. 2004), aff'd, 389 F.3d 1272 (2004) ("'dangerous consequences would flow' if an ANDA applicant has an unqualified right to become effective at a date in the future") (quoting *Barr Labs. Inc. v. Thompson*, 238

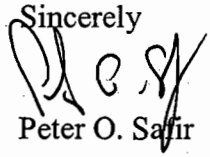
[2] The fact that section 355(j)(5)(B)(iii)(II)(aa)(AA) uses the same substantive language ("date on which the court of appeals decides") as the provision it replaced ("date of the court's decision," former 21 U.S.C. § 355(j)(5)(B)(iii)(I)), is further reason FDA should continue to apply the approach articulated in its 2000 guidance document.

F.Supp.2d 236, 249 (D.D.C. 2002)). Thus, as of the date of patent expiry Apotex will have only a tentative approval and in accordance with the decision in *Ranbaxy Labs. Ltd. v. FDA*[3] , and pediatric exclusivity will attach.

Conclusion

As set forth herein, FDA should not grant full approval to Apotex's ANDA for amlodipine. Such approval is prohibited by a district court order, and is not affected by the Federal Circuit's March 22 opinion. Thus, FDA should withhold any action regarding Apotex's ANDA unless and until a mandate issues from the Federal Circuit reversing or vacating the district court's order.

Sincerely



Peter O. Safir

cc: Jeffrey B. Chasnow
Pfizer Inc

[3] 307 F.Supp.2d 15, 21 (D. D.C. 2004), *aff'd*, 96 Fed. Appx. 1 (D.C. Cir. 2004),