ORAL ARGUMENT TO BE SCHEDULED

Consolidated Case Nos. 10-5094, 10-5108

In The United States Court of Appeals For The District of Columbia Circuit

APOTEX, INC. & ROXANE LABS., INC.,

Plaintiffs/Appellants,

v.

KATHLEEN SEBELIUS, ET AL.,

Defendants/Appellees,

TEVA PHARMACEUTICALS USA, INC.,

Intervenor-Defendant/ Appellee.

On Appeal from the United States District Court for the District of Columbia (Nos. 09-517, 09-521, Judge Rosemary M. Collyer)

BRIEF OF APPELLEE TEVA PHARMACEUTICALS USA, INC.

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May 18, 2010

CORPORATE DISCLOSURE STATEMENT

Pursuant to Fed. R. App. P. 26.1, Teva Pharmaceuticals USA, Inc. states as follows:

Teva Pharmaceuticals USA, Inc. is a Delaware corporation with its principal place of business and corporate headquarters in North Wales, Pennsylvania. Teva Pharmaceuticals USA, Inc. is a wholly owned, indirect subsidiary of Teva Pharmaceutical Industries Ltd. No other publicly held corporation owns 10% or more of its stock.

May 18, 2010

/s Michael D. Shumsky
Michael D. Shumsky

Counsel for Appellee
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CERTIFICATE AS TO PARTIES, RULINGS AND RELATED CASES

Parties and *Amici*. Appellants Apotex, Inc. ("Apotex") and Roxane Laboratories, Inc. ("Roxane") were the plaintiffs in the district court. Appellees Kathleen Sebelius, in her official capacity as Secretary of Health and Human Services; Margaret Hamburg, M.D., in her official capacity as Commissioner of Food and Drugs; the U.S. Food and Drug Administration; and the U.S. Department of Health and Human Services were the defendants in the district court (collectively, "FDA"). Appellee Teva Pharmaceuticals USA, Inc. ("Teva") was an intervenor-defendant in the district court. Zydus Pharmaceuticals USA, Inc. filed an *amicus* brief in the district court.

Rulings Under Review. On April 2, 2010, the district court (Collyer, J.) denied Roxane and Apotex's motions for preliminary injunctive relief. A copy of the district court's unpublished opinion can be found at A11-17, and its accompanying order can be found at A18.

Related Cases. This case is related to *Teva Pharms. USA, Inc. v. Sebelius*, consolidated case Nos. 09-5281 and 09-5303, which resolved Teva's entitlement to 180-day exclusivity for the same drug product at issue in this case, involved virtually all of the parties to this litigation,

and specifically considered the issue now raised by the plaintiffs-appellants during post-judgment proceedings regarding the issuance of its mandate. FDA filed a petition for panel rehearing and rehearing *en banc* in that case, which was denied on May 17, 2010.

May 18, 2010

/s Michael D. Shumsky
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GLOSSARY

'075 Patent	U.S. Patent No. 5,608,075
180-Day Exclusivity	Period of marketing exclusivity awarded to the first generic applicant that submits an ANDA containing a Paragraph IV certification to a patent listed in the Orange Book
A	Joint Appendix
ANDA	Abbreviated New Drug Application
Apotex	Plaintiff/Appellant Apotex, Inc.
FDA	Food and Drug Administration
Hatch-Waxman Act	Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585
Merck	Merck & Co., Inc.
MMA	Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066
NDA	New Drug Application
Orange Book	*Approved Drug Products with Therapeutic Equivalence Evaluations*
Paragraph IV Certification	A certification that a patent listed in the Orange Book is invalid, unenforceable, or not infringed by the generic drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).
PTO	U.S. Patent and Trademark Office

Roxane	Plaintiff/Appellant Roxane Labs., Inc.
Teva	Defendant/Appellee Teva Pharms. USA, Inc.

INTRODUCTION AND SUMMARY OF THE ARGUMENT

On March 2, this Court squarely rejected brand manufacturer Merck's attempt to manipulate the statutory incentive for challenging its patents by unilaterally "delisting" the '075 patent from FDA's Orange Book and thereby divesting Teva of exclusivity. *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303 (D.C. Cir. 2010). As *Teva* explained in no uncertain terms, there is "*not a single cogent reason* why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity," *id.* at 1317 (emphasis original), nor any "reason to conclude that the 2003 addition of [the statute's] forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity." *Id.* at 1318.

To its credit (and despite its disagreement with *Teva*), FDA properly recognized that *Teva*'s *Chevron* step one analysis of the statute's incentive structure forecloses plaintiffs' thirteenth-hour attempt to evade Teva's exclusivity. If Merck cannot "'unilaterally' divest [Teva] of its exclusivity [by] delisting" the '075 patent, it cannot "'unilaterally' divest [Teva] of its exclusivity" through the simple artifice

of ceasing to pay maintenance fees on that patent. A92 (quoting *Teva*, 595 F.3d at 1305, 1318). Any other outcome would be absurd: It would allow Merck to achieve through the back door (by not paying maintenance fees on the '075 patent) precisely what it is barred from achieving through the front door (by delisting that patent), and thus would sanction Merck's belt-and-suspenders attempt to eviscerate Teva's exclusivity despite the lack of "*a single cogent reason* why Congress might have permitted [Merck to] unilaterally deprive [Teva] of its exclusivity." *Teva*, 595 F.3d at 1317 (emphasis original).

As a result, plaintiffs now take the only tack they can: They argue that FDA should have ignored *Teva*'s analysis of the statute's incentive structure, Br. at 17-30, and contend that this "Court need not and we submit should not adopt" *Teva*'s analysis because in that case "policy considerations were allowed to override the plain language of the statute." Br. at 15. That argument is frivolous. Federal agencies are bound to apply the law regardless of whether it is set forth in statutes or court cases interpreting those statutes at *Chevron* step one. If, as plaintiffs assert, it was wrong for FDA to account for this Court's *Chevron* step one analysis of the same statutory scheme, then every

agency stands condemned—and "judicial review of agency action [would become] a ping-pong game," *George Hyman Constr. Co. v. Brooks*, 963 F.2d 1532, 1539 (D.C. Cir. 1992) (quotation omitted), in which agencies not only are free—but in fact are compelled—to ignore relevant precedents with which they disagree. This Court should reject plaintiffs' invitation to essentially write *Teva* out of existence.

But even if the merits were close, this is an appeal from the denial of a preliminary injunction—not from a final judgment on the merits. Accordingly, this Court can reverse only if it concludes that the district court abused its discretion in balancing plaintiffs' slim likelihood of success against the equities. Plaintiffs nonetheless devote just two pages to those factors, and for good reason: The equities uniformly favor Teva. In short, plaintiffs seek to compel immediate FDA approval of their ANDAs, which irreparably would eviscerate Teva's exclusivity before the merits definitively are resolved. To justify that extraordinary relief, however, plaintiffs have asserted only that they stand to lose a combined maximum of $38.6 million if Teva maintains exclusivity. Even if those purely monetary losses were cognizable as irreparable harm (which they aren't), the requested injunction irreparably would

cause Teva to lose both its statutory right to exclusivity and, as *Teva* recognized, literally "hundreds of millions of dollars." 595 F.3d at 1314. The balance of hardships thus decisively favors Teva.

Perhaps most important, however, the public interest sharply weighs against relief. As *Teva* again recognized:

> The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device [which] deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by the promise of a reward for generics that stick out their necks … by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted.

Id. at 1318. Divesting Teva of its exclusivity thus would stall the engine that drives challenges to competition-blocking patents, in direct contravention of the statute's "pro-consumer" objectives.

At bottom, this is not a close case, and FDA's decision only underscores how clear it is. While that decision sharply criticizes *Teva*, FDA nonetheless found itself compelled to conclude that unilateral patent delistings and unilateral patent terminations are two sides of the same coin—and thus equally foreclosed by *Teva*'s analysis of the statute's incentive scheme. If there were a sensible way to split that

coin in half, the tenor of FDA's letter decision makes clear the Agency would have found it. But FDA did not do so—because it could not do so—and the district court's decision should be affirmed.

STATEMENT OF JURISDICTION

Plaintiffs' jurisdictional statement is complete and accurate.

STATEMENT OF THE ISSUE

Did the district court abuse its discretion in denying preliminary injunctive relief?

STATEMENT OF THE CASE

A. The Hatch-Waxman Framework

As modified by the Medicare Modernization Act ("MMA"), the Hatch-Waxman Act establishes the procedure for obtaining drug approvals. 21 U.S.C. § 355 *et seq*. That statute requires the manufacturer of a brand-name drug to complete a New Drug Application ("NDA") that contains clinical data demonstrating the proposed drug's safety and efficacy, *id.* § 355(b)(1), and information about each patent the applicant asserts as claiming that drug (including its number and scheduled expiration date). *Id.* § 355(b)(2); 21 C.F.R. § 314.50(h); *id.* § 314.53(b).

Generic drugs contain the same active ingredients and provide the same benefits as their brand-name counterparts, but typically are sold at lower prices. Before Hatch-Waxman, generic manufacturers had to complete a full NDA to obtain approval—making generic market entry cost-prohibitive. In 1984, Congress enacted Hatch-Waxman to remove that barrier, increase the availability of generic drugs, and reduce pharmaceutical costs. *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1326 (D.C. Cir. 1998).

To that end, Hatch-Waxman authorizes FDA approval if a generic applicant can demonstrate its product's bioequivalence to a "listed" (or previously approved) brand-name drug. Generic applicants do so by submitting an Abbreviated New Drug Application ("ANDA") that includes studies demonstrating bioequivalence. 21 U.S.C. § 355(j). If FDA accepts those studies, the generic applicant need not replicate the brand's prior clinical studies. *Id.* § 355(j)(2)(A); *see also Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998).

The statute also requires each ANDA to include a "certification" for every patent the brand manufacturer listed for the brand-name drug. *Id.* § 355(j)(2)(A)(vii). To make this system work, the statute

requires FDA to "publish" the patent information it receives from brand manufacturers. *Id.* § 355(j)(7)(a)(i)-(iii). FDA's official patent register is known as "the Orange Book." *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 880 (D.C. Cir. 2004).

Generic applicants must make one of four certifications: (1) that no patent information was filed for the brand-name drug ("Paragraph I certification"); (2) that a listed patent "has expired" ("Paragraph II certification"); (3) that the generic drug will not be marketed until "the date on which [a listed] patent will expire" ("Paragraph III certification"); or (4) that a listed patent is invalid, unenforceable, and/or will not be infringed by the proposed generic drug ("Paragraph IV certification"). 21 U.S.C. § 355(j)(2)(A)(vii).

Paragraph IV certifications play a key role in the statutory scheme. They signal the generic's intent to market its products before the scheduled expiration of a listed patent, and thus that the applicant intends to provide consumers with expedited price relief. *Teva Pharms. USA, Inc. v. Leavitt* ("*Teva v. Leavitt*"), 548 F.3d 103, 106 (D.C. Cir. 2008) ("The legislative purpose underlying paragraph IV is to enhance competition by encouraging generic drug manufacturers to challenge

the patent information provided by NDA holders in order to bring generic drugs to market earlier.").

But filing such a certification is risky. The first challenger bears significant research-and-development and legal costs to design around and/or contest the validity of a listed patent. If those efforts succeed, the very act of submitting a Paragraph IV certification is an act of patent infringement that could require the applicant to spend years defending itself in patent litigation. 35 U.S.C. § 271(e); *see also Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 678 (1990).

To encourage generics to accept those risks, the statute rewards the first patent challenger with a 180-day period of marketing exclusivity. *Teva v. Leavitt*, 548 F.3d at 104 ("Marketing exclusivity is valuable, designed to compensate manufacturers for research and development costs as well as the risk of litigation."). In some cases (as here), that reward is worth "hundreds of millions of dollars." *Teva*, 595 F.3d at 1314.

Pursuant to the MMA, the first generic applicant nonetheless can "forfeit" its exclusivity in certain circumstances. 21 U.S.C. § 355(j)(5)(D)(i). Two circumstances are relevant here. First, the first

generic applicant can forfeit exclusivity if it fails promptly to market its products after certain events—including (in general terms) a successful outcome in patent litigation, or after the brand manufacturer withdraws (or "delists") a patent from the Orange Book. *Id.* § 355(j)(5)(D)(i)(I). This provision is known as the "failure-to-market" forfeiture trigger.

Second, the first applicant may forfeit exclusivity if "[a]ll of the patents as to which the applicant submitted a [Paragraph IV certification] have expired." *Id.* § 355(j)(5)(D)(i)(VI). That provision of the statute codified FDA's longstanding practice of rejecting exclusivity where the first applicant failed to begin marketing before the challenged patent expired *naturally—i.e.*, at the end of its scheduled term. *See Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 354-55 (D.N.J. 2003); FDA Letter Decision No. 99P-1271 ("Cisplatin Decision"), 4 (Aug. 2, 1999).

B. The Delisting Rule

Shortly after Congress passed Hatch-Waxman, brand companies realized that delisting a challenged patent—instead of defending it in litigation—could eliminate the first applicant's exclusivity period and

thereby undercut the incentive for generic applicants to challenge branded patents. That was so because generic applicants can certify only to patents listed in the Orange Book, and can only receive exclusivity if they maintain a lawful Paragraph IV certification. 21 U.S.C. § 355(j)(5)(B)(iv) (2002); *id.* § 355(j)(5)(B)(iv)(II)(bb) (2003). FDA acquiesced in that practice, and brand companies routinely began delisting challenged patents in order to undercut the incentive for patent challenges.

Teva challenged that manipulative practice, and this Court rejected FDA's acquiescence in it at *Chevron* step one. *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 126 (D.C. Cir. 2006). As *Ranbaxy* explained, FDA's delisting policy eviscerated the exclusivity reward, because it allowed brand companies strategically to "reduce[e] the certainty of receiving a period of marketing exclusivity" and thereby "diminish[] the incentive for [generics] … to challenge a [listed] patent." *Id.* at 126.

Ranbaxy, however, was decided before the MMA. And seizing upon the MMA's new "failure-to-market" forfeiture provision—which in certain circumstances provides for forfeiture where a patent is delisted,

21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC)—FDA announced that *Ranbaxy* did not survive the MMA. *Teva*, 595 F.3d at 1306. Instead, according to FDA, "[b]rand manufacturers are [now] free to delist challenged patents *whenever* they please—and any such delisting [causes a forfeiture]." *Id.* at 1315 (emphasis added). This approach was known as the "Delisting Rule."

C. Losartan Potassium Products

Losartan potassium is an antihypertensive agent. Merck holds two NDAs relating to losartan potassium, which it markets as Cozaar® and Hyzaar®. When those drugs were approved, Merck listed the same three patents[1] in the Orange Book for both: U.S. Patent No. 5,138,069 ("the '069 patent"), which was scheduled to block competition through February 11, 2010; U.S. Patent No. 5,153,197 ("the '197 patent"), which was scheduled to block competition through April 6, 2010; and U.S. Patent No. 5,608,075 ("the '075 patent"), which was scheduled to block competition through September 4, 2014.[2]

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[1] Merck also listed a fourth patent for Cozaar® NDA, but that patent relates to a method of treatment for which Teva did not seek approval.

[2] Each patent actually expires six months before these dates. However, Merck earned a six-month period of "pediatric exclusivity" which prevented FDA from (Continued…)

On December 18, 2003, Teva submitted an ANDA for generic Cozaar®. FDA accepted that ANDA on February 11, 2004. Teva's ANDA contained Paragraph III certifications to the '069 and '197 patents, meaning that it would not seek to market its products until the '197 patent's scheduled expiration on April 6, 2010. However, Teva also submitted a Paragraph IV certification to the '075 patent, claiming that that patent is invalid, unenforceable, and/or would not be infringed by Teva's products—and thus that Teva intended to begin marketing its products years before that patent's scheduled expiration in 2014. Teva was the first generic applicant to challenge the '075 patent. *Teva*, 595 F.3d at 1307.

On May 24, 2004, Teva submitted an ANDA for generic Hyzaar®. FDA accepted that ANDA on July 15, 2004. That ANDA contained the same certifications as Teva's Cozaar® ANDA—including a Paragraph IV certification to the '075 patent signaling Teva's intent to market its generic Hyzaar® years before that patent's scheduled expiration in

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approving ANDAs for these drugs until six months after each patent expires. 21 U.S.C. § 335a. Absent a Paragraph IV challenge, these three patents thus would have blocked generic competition until September 4, 2014.

2014. Once again, Teva was the first generic Hyzaar® applicant to challenge the '075 patent. *Id.*

As the first patent-challenging applicant, Teva became eligible for 180-day exclusivity on both drugs. *Teva*, 595 F.3d at 1307. Teva then notified Merck of its challenges, explaining that most of the '075 patent's claims were invalid based on prior art and that Teva's generic losartan products did not infringe the patent's remaining claims under the doctrine of equivalents.

Merck did not sue Teva. Instead, in March 2005—*after* Teva submitted its exclusivity-qualifying Paragraph IV certifications to the '075 patent—"Merck asked the FDA to delist" the '075 patent from the Orange Book, "which the agency did." *Id.* at 1307. Then, *after* asking FDA to delist the '075 patent, Merck apparently stopped paying maintenance fees on that patent. A13; *see also* 35 U.S.C. § 41(b) (requiring maintenance fees).

By delisting the '075 patent, Merck effectively conceded that Teva's Paragraph IV certification was so strong that Merck could not reasonably assert that patent against any generic applicant, and thus that Merck could not lawfully use that patent to block competition.

Teva thus accomplished precisely what Congress sought to reward: It identified a competition-blocking patent, invested the resources needed to challenge it, and successfully removed it as a barrier to competition—thereby opening the market to generic entry more than four years earlier than would have been possible without Teva's challenge. Under FDA's Delisting Rule, however, Teva "had by the fall of 2008 *already* forfeited" its exclusivity because of Merck's unilateral decision to delist the '075 patent. *Teva*, 595 F.3d at 1308 (emphasis original).

D. The *Teva* Litigation

Attacking the Delisting Rule as unlawful, Teva sued FDA and sought relief intended to protect its 180-day exclusivity period. Teva also sought a preliminary injunction, explaining that it would be harmed irreparably absent prompt judicial review. The district court consolidated Teva's request for preliminary injunctive relief with a trial on the merits, but entered judgment for FDA. *Id*. at 1305.

On March 2, this Court reversed—invalidating the Delisting Rule "at *Chevron* step one," *id.* at 1318, and repeatedly explaining that there is "no reason to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a

generic's exclusivity." *Id.* at 1318; *see also id.* at 1317 ("The agency … *offers not a single cogent reason* why Congress might have … provided for a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity.") (emphasis original); *id.* at 1318 ("[N]othing in the 2003 amendments to the Food, Drug, and Cosmetic Act … changes the structure of the statute such that brand companies should be newly able to delist challenged patents, thereby triggering a forfeiture event that deprives generic companies of the period of marketing exclusivity they otherwise deserve."). This Court then remanded the case for the entry of appropriate relief, *id.* at 1319, but simultaneously entered a routine administrative order withholding the mandate until 7 days after FDA's deadline for seeking rehearing.

E. Post-Judgment Proceedings

Because that routine order would have prevented the district court from acting on remand *before* FDA could have approved other applicants, Teva requested immediate issuance of the mandate. Emer. Mot. To Issue Mandate ¶¶ 4-7, *Teva* (Mar. 9, 2010).

That same day, however, Apotex apparently informed FDA that Merck's '075 patent may have prematurely expired *in March 2009* due

to Merck's failure to pay maintenance fees. Citing that development, FDA then opposed Teva's motion. FDA Opp., *Teva* (Mar. 11, 2010). In particular, FDA asserted (like plaintiffs here) that Merck's unilateral decision to cease paying maintenance fees meant that "a forfeiture event other than the delisting of the '075 patent—namely, expiration of a patent that is the subject of a paragraph IV certification[—]… has, in fact, occurred." *Id.* at 7.

Teva replied that the *Teva* decision itself squarely foreclosed FDA's new argument. Rep. in Supp. of Emer. Mot., *Teva* (Mar. 12, 2010). Noting that "brand manufacturers routinely stop paying the fees on patents they have delisted," *id.* at 11 & n.2 (collecting examples), Teva argued that FDA's effort to divorce Merck's unlawful delisting request from its subsequent failure to pay maintenance fees

> boils down to the absurd proposition that brand manufacturers somehow are allowed to achieve through the back door (by not paying maintenance fees on a challenged patent) precisely what this Court's decisions in both this case and *Ranbaxy* forbid them from doing through the front door (by delisting the challenged patent in the first place). As [*Teva*] recognized, however, there is 'not a single cogent reason why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity,' and that judgment is controlling here.

Id. at 11 (quoting *Teva*, 595 F.3d at 1317). After considering these submissions, this Court on March 12 granted Teva's motion to issue the mandate forthwith.

F. The *Teva* Remand

On March 16, the district court held that this Court's consideration of the patent-expiration issue in post-judgment proceedings foreclosed new litigation over that issue, and therefore enjoined FDA "from approving any [ANDA] for a generic [losartan product] prior to the conclusion of Teva's 180-day period of marketing exclusivity." *Teva Pharms. USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 28 (D.D.C. Mar. 16, 2010). On March 26, however, the district court reconsidered that decision, *id.*, dkt. 33 (Mar. 26, 2010), and noted that any challenge to FDA's administrative decision on this issue could be raised "in a new lawsuit." *Id.* at 3 n.4.

G. FDA's Letter Decision

On March 26, FDA issued the decision giving rise to this litigation. Although that decision vigorously disputed *Teva*'s analysis, it nonetheless held that *Teva*'s reasoning "appears to preclude a forfeiture of exclusivity on the basis of a patent expiration where the

expiration is in the control of the NDA holder." A92. It therefore declared that FDA "will not approve any other [losartan] ANDA until [Teva] has received approval of its ANDA, begun commercial marketing, and the 180-day exclusivity period has expired." A93.

Plaintiffs then sought preliminary injunctive relief that would bar FDA from awarding Teva exclusivity and compel FDA to approve their ANDAs immediately. A19-42. On April 2, the district court denied plaintiffs' motions. On the merits, it explained that FDA did not err "when it politely expressed its disagreement with a D.C. Circuit decision that had ruled against the agency, but nonetheless applied the reasoning of the Circuit to a different but, on these facts, closely related question." A15. On the equities, it explained that plaintiffs' purely economic injuries did not constitute irreparable harm, A15-16; that the requested relief "would certainly injure Teva," A16; and that the public interest weighed against relief given the exclusivity reward's "'pro-consumer'" goals. *Id.* (quoting *Teva*, 595 F.3d at 1318).

On April 5, Apotex sought a stay of all FDA approvals and summary reversal of the district court's decision. On April 6, this Court denied Apotex's motion for summary reversal without even waiting for

a response, and likewise denied the stay. FDA thus approved Teva's losartan ANDAs, and Teva began marketing its products. Roxane then noticed its appeal. This Court consolidated plaintiffs' appeals, and this expedited briefing followed.

STANDARD OF REVIEW

The standard for preliminary injunctive relief is well-settled. "A plaintiff seeking a preliminary injunction must establish that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest." *Winter v. NRDC*, 129 S. Ct. 365, 374 (2008). Although "[t]hese factors interrelate on a sliding scale and must be balanced against each other," *Davenport v. IBT*, 166 F.3d 356, 360-61 (D.C. Cir. 1999), "a movant cannot obtain a preliminary injunction without showing *both* a likelihood of success *and* a likelihood of irreparable harm." *Davis v. Pension Ben. Guar. Corp.*, 571 F.3d 1288, 1296 (D.C. Cir. 2009) (Kavanaugh and Henderson, JJ., concurring) (emphasis original). Where "substantial harm to the nonmovant is very high and the

showing of irreparable harm to the movant very low, the movant must demonstrate a much greater likelihood of success." *Id.* at 1292.

In turn, the question "whether a preliminary injunction should be awarded rests in the sound discretion of the trial court," *Ambach v. Bell*, 686 F.2d 974, 979 (D.C. Cir. 1982), and thus cannot be reversed except for abuse of that discretion. Such deference is warranted because the denial of injunctive relief typically is based on equitable factors that best are considered by the trial court. *Friends For All Children, Inc. v. Lockheed*, 746 F.2d 816, 834-35 & n.32 (D.C. Cir. 1984); *WMATA Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 842 (D.C. Cir. 1977).

ARGUMENT

I. Plaintiffs Have No Likelihood Of Success.

FDA finally got it right. *Teva*'s "'*Chevron* step one'" interpretation of "the structure of the MMA exclusivity provisions … does not permit an NDA holder to 'unilaterally' deprive the generic applicant of its exclusivity," and that reasoning applies no less to Merck's unilateral attempt to deprive Teva of exclusivity by abandoning the '075 patent through non-payment of maintenance fees than it does to Merck's antecedent attempt to deprive Teva of exclusivity by delisting that

patent. A92-93 (quoting *Teva*, 595 F.3d at 1305, 1317); *see also Teva*, 595 F.3d at 1318 (holding there is "no reason to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity"); *Ranbaxy*, 469 F.3d at 126 ("FDA may not, however, change the incentive structure [by] allow[ing] an NDA holder … to deprive the generic applicant of a period of marketing exclusivity.").

FDA thus reached the only conclusion it could. Because Merck cannot unilaterally divest Teva of exclusivity by delisting the '075 patent in response to Teva's challenge, Merck cannot unilaterally divest Teva of exclusivity by artificially pretermitting that patent's natural term in response to Teva's challenge. Any other result would eviscerate both the statutory incentive to challenge competition-blocking patents and Hatch-Waxman's outright bar against manipulative patent delistings (which *Teva* and *Ranbaxy* recognized *at* Chevron *step one*, *see Teva*, 595 F.3d at 1318; *Ranbaxy*, 469 F.3d at 125-26), by freely allowing

brand manufacturers to achieve with one hand precisely what the statute precludes them from doing with the other.[3]

Plaintiffs' core response to this straightforward point is easily summarized: The statute provides for forfeiture where all exclusivity-qualifying patents "have expired," Br. at 17-24 (discussing 21 U.S.C. § 355(j)(5)(D)(i)(VI)); the patent laws in turn provide that a patent "expires" after the patentee fails to pay maintenance fees, Br. at 25-26 (discussing 35 U.S.C. § 41(b)); and, thus, "this Court should enforce the statute according to its terms and without engaging in further inquiry," *id.* at 29—that is, that this Court "need not and we submit should not adopt" *Teva*'s analysis because the *Teva* panel "allowed … policy considerations to override the [statute's] plain language." *Id.* at 15.

That argument is deeply flawed, beginning with its approach to statutory interpretation. As the Supreme Court long has explained, "the meaning of statutory language, plain or not, depends on context."

[3] Indeed, as Teva explained to both FDA and this Court in *Teva*, brand manufacturers routinely cease paying maintenance fees on previously delisted patents. *See* Comments of Teva Pharmaceuticals USA, Inc., FDA Docket No. 2010-FDA-0134, at 3 & n.1 (filed Mar. 18, 2010), *available at* http://www.regulations.gov/search/Regs/contentStreamer?objectId=0900006480abfc71&disposition=attachment&contentType=pdf (last visited May 18, 2010).

King v. St. Vincent's Hosp., 502 U.S. 215, 221 (1991); *see also Johnson v. United States*, 130 S.Ct. 1265, 1270 (2010) ("Ultimately, context determines meaning."); *Robinson v. Shell Oil Co.*, 519 U.S. 337, 341 (1997). While plaintiffs thus are correct that statutory interpretation begins (and often ends) with the statute's "plain language," Br. at 17, *the meaning* of that language can only be determined—as *Teva* itself recognized, 595 F.3d at 1315—by reference to the statute's whole text, structure, and place in the law (including its relationship to pertinent judicial decisions). *Dolan v. USPS*, 546 U.S. 481, 486 (2006) ("Interpretation of a word or phrase depends upon reading the whole statutory text, considering the purpose and context of the statute, *and consulting any precedents or authorities that inform the analysis*.") (emphasis added).

FDA thus did not remotely err by conforming its decision to *Teva*'s *Chevron* step one analysis of the statute's incentive structure. Indeed, the implications of plaintiffs' argument are staggering. By their reasoning, federal agencies not only are free to ignore pertinent judicial decisions with which they disagree, but *are compelled* to do so; as Apotex forthrightly expressed this argument below: "The agency may

not reach a result that … *it itself* concludes is 'inconsistent with the plain language of the statute.' To do so is the very embodiment of an arbitrary and capricious decision." Apotex Dist. Ct. Br. at 11 (emphasis added).

The district court properly rejected that remarkable claim. Whether plaintiffs like it or not, FDA was obligated to consider the controlling law of this Circuit. Plaintiffs are free to echo FDA's disdain for *Teva*'s *Chevron* step one analysis, but they cannot sensibly fault FDA for consistently applying it here. A15 ("The Court cannot find that FDA was arbitrary or capricious when it politely expressed its disagreement with [*Teva*], but nonetheless applied the reasoning of the Circuit to a … closely related question."); *see also United Savings Ass'n v. Timbers of Inwood Forest Assocs.*, 484 U.S. 365, 371 (1988) ("Statutory construction … is a holistic endeavor. A provision that may seem ambiguous in isolation is often clarified … *because only one of the permissible meanings produces a substantive effect that is compatible with the rest of the law*.") (emphasis added).

Plaintiffs' patent-law argument fares no better. While it is true that the patent laws provide that a patent can "expire" if the patentee

fails to pay maintenance fees, 35 U.S.C. § 41(b), and that "'[t]here is a presumption that Congress uses the same term consistently in different statutes,'" Br. at 25 (quoting *NTEU v. Chertoff*, 452 F.3d 839, 857-58 (D.C. Cir. 2006), this argument has only superficial appeal. As the Supreme Court long has warned, that "'presumption is not rigid and readily yields whenever there is such variation in the connection in which the words are used as reasonably to warrant the conclusion that they were employed … with different intent.'" *Gen. Dynamics Land Sys., Inc. v. Cline*, 540 U.S. 581, 595 & n.8 (2004) (quoting *Atl. Cleaners & Dyers v. United States*, 286 U.S. 427, 433 (1932)). Indeed, the Court routinely complains that the "tendency to assume that a word which appears in two or more legal rules … should have precisely the same scope in all of them … has all the tenacity of original sin and must constantly be guarded against." *Id.* (quotation omitted; collecting authorities).

Accounting for Hatch-Waxman's particular context is dispositive here. Indeed, Roxane expressly conceded the point below:

> If the reasoning in *Teva* were to be applied to the patent expiration forfeiture provision, FDA would be required, *based on the incentive structure for 180-day exclusivity designed by Congress*, to interpret the term expired in the

> forfeiture provision as not including expiration of a patent for failure to pay maintenance fees. *To do otherwise would allow the brand manufacturer to unilaterally deprive the generic manufacturer of 180-day exclusivity in contravention of the incentive structure.*

Roxane Dist. Ct. Br. at 16 (emphasis added); *see also Teva*, 595 F.3d at 1318 (holding that there is "no reason to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity."). That explains why Roxane candidly (if baselessly) argued below that interpretation of the word "'expiration' should reflect the use of that term in patent law" *without reference to* "the context of Hatch-Waxman." Roxane Dist. Ct. Br. at 15.

Even beyond their *conceded* incompatibility with the statute's incentive structure, there are three additional reasons for declining to import unilateral patent-term truncations into the Hatch-Waxman context. First, Hatch-Waxman's other references to patent expiration demonstrate that Congress was concerned only with natural patent expiration in this statute. In particular, where an applicant files a Paragraph III certification, the statute requires it to state at the time it files its ANDA "the date on which [the listed] patent *will expire*." 21

U.S.C. § 355(j)(2)(A)(vii)(III) (emphasis added). But if patents can, for Hatch-Waxman purposes, "expire" for non-payment of fees, Paragraph III would be meaningless: Because the brand manufacturer could quit paying its fees at any time, generic applicants could only guess what date to include in such a certification; it would be impossible to predict that date with certainty, since on plaintiffs' view it is subject entirely to the brand company's caprice. By contrast, the only date generic applicants can state with any certainty is the date the patent *is scheduled to expire—i.e.*, the patent's natural expiration date—and that, of course, is the date that counts in this context.

Second, unlike patents that expire naturally, patents which PTO treats as expiring for non-payment of maintenance fees don't actually die. Instead, such patents can be revived, in some cases "at any time." 35 U.S.C. § 41(c)(1) ("The Director may accept the payment of any maintenance fee required … within [24] months after the six-month grace period if the delay [was] unintentional, or at any time after the six-month grace period if the delay [was] unavoidable…. If the Director accepts payment … *the patent shall be considered as not having expired*.") (emphasis added).

Requiring forfeiture upon a patentee's unilateral failure to pay maintenance fees thus not only would allow brand companies to *deliberately* strip the first generic's exclusivity in direct contravention of the statute's incentive structure (as plaintiffs now concede happened here, Br. at 26 n.4), but would allow brand manufacturers to do so *negligently*. In particular, after an inadvertent lapse in payment and consequent forfeiture, plaintiffs' interpretation would allow FDA to approve all ANDAs immediately—leaving the first applicant without recourse if the patent later is revived and thus treated "as not having expired," 35 U.S.C. § 41(c)(1). *See Teva*, 595 F.3d at 1311 (once subsequent applicants are approved, the first filer suffers "an injury that would not be remedied by … securing 180 days of exclusivity later on"). Congress could not possibly have intended that absurd result.

Finally, and perhaps most important, the rationale for divesting the first applicant of exclusivity based on patent expiration does not remotely apply where the brand manufacturer artificially pretermits a patent's natural term. Long before the MMA added this forfeiture trigger, FDA interpreted the statute to preclude exclusivity after a patent expired naturally. *See Dr. Reddy's Labs., Inc. v. Thompson*, 302

F. Supp. 2d 340, 354-55 (D.N.J. 2003); Cisplatin Decision at 4. The basis for that approach is simple. Paragraph IV certifications are designed to expedite generic competition. *Teva v. Leavitt*, 548 F.3d at 106. But where the first applicant does not launch before the challenged patent expires *on its own*, the applicant's certification has accomplished nothing. *Dr. Reddy's*, 302 F. Supp. 2d at 354 ("Once a listed patent expires, there is no longer a need to provide an incentive to challenge it."). That principle also explains why FDA does not allow applicants to maintain a Paragraph IV certification if they do not intend to launch their products before a challenged patent's scheduled expiration (and thus accomplish nothing by their certification), and why FDA likewise does not award exclusivity where an applicant loses its patent case (and likewise accomplished nothing by its certification).

By contrast, when a patent lapses not by the mere passage of time, *but rather because the first applicant's Paragraph IV certification caused the patentee to abandon its patent*, the applicant's challenge has accomplished precisely what the statute rewards: It has opened the market to competition years earlier than would have been possible absent that challenge. There is thus no reason to think Congress

intended *to extend* to these circumstances (rather than simply *to codify*) FDA's prior practice of stripping exclusivity following a patent's *natural* expiration, and every reason to conclude that Teva earned its exclusivity here.

After all, Teva made enormous investments to challenge the '075 patent's validity and engineer a non-infringing pathway around any claims not subject to such a challenge. Those investments yielded a Paragraph IV certification so strong that Merck simply gave up—first by delisting that patent, and then by ceasing to pay maintenance fees. Teva's challenge thereby cleared the path for generic competition to begin on these $1.5-billion-per-year drugs *four years earlier* than it could have without Teva's certification, and thus will save consumers literally billions of dollars between April 6, 2010 (when Teva launched) and September 4, 2014. There is no sensible basis for allowing Merck to punish Teva for delivering those savings to American consumers.

Plaintiffs nonetheless argue that it is reasonable to require forfeiture under these circumstances, asserting that exclusivity:

> *is designed to encourage generic companies to litigate against patents* that block generic entry to the market but which could be held invalid or not to infringe in litigation. If the patent has expired, there can be no patent lawsuit, and thus

> there would be no reason for Congress to provide the 180-day exclusivity period in this context.

Br. at 23 (emphasis added).

But exclusivity is not intended *to encourage litigation*; it is intended to enable *early generic competition*. That's why this Court *repeatedly* has rejected attempts to condition exclusivity on the presence or absence of litigation. *Ranbaxy*, 469 F.3d at 125; *Purepac*, 162 F.3d at 1204-05; *Mova*, 140 F.3d at 1069-70. As these cases recognize, a Paragraph IV certification that bloodlessly enables early market entry because the brand manufacturer waives the white flag is no less deserving of reward than if it achieved the same result through costly and time-consuming litigation. *Ranbaxy*, 469 F.3d at 125 ("Not only does the statute not require litigation to preserve a generic applicant's eligibility for exclusivity, as [our] precedents make clear; such a requirement is inconsistent with the structure of the statute.").

One final point is in order. Plaintiffs assert that "the only possible certification [in this case] is a paragraph II certification that the patent has expired," Br. at 21, "which explains why [FDA] permitted appellants to change their certifications from paragraph IV to paragraph II." *Id.* at 23. Indeed, plaintiffs argue, FDA's analysis

means that "under the forfeiture provision, a patent would not be considered to have 'expired" … while under the certification provisions a patent would be considered to have 'expired.'" *Id*. at 24.

Those assertions are meritless. The merits issue in this case ultimately boils down to the question of whose certifications are valid: Teva's Paragraph IV certifications or plaintiffs' Paragraph II certifications. If defendants are right that the '075 patent has not expired for Hatch-Waxman purposes, plaintiffs will have to re-certify under Paragraph IV. Contrary to plaintiffs' assertion, there would be nothing improper about such a certification: It appropriately would signify that plaintiffs intend to market their products prior to the '075 patent's natural expiration date in 2014. By contrast, if plaintiffs are correct that artificial patent-term terminations count for Hatch-Waxman purposes, Teva will be forced to recertify under Paragraph II. Plaintiffs' assertion that FDA's decision somehow creates an internal inconsistency within the law thus merely begs the question.

At bottom, every decisionmaker that has considered these claims has ruled in Teva's favor—the *Teva* panel, when in post-judgment proceedings it considered and implicitly rejected FDA's initial argument

that "a forfeiture event other than the delisting of the '075 patent … has, in fact, occurred"; FDA, when it issued its March 26 letter decision; and the district court, when it rejected plaintiffs' motions for preliminary injunctive relief. Plaintiffs' fourth bite at the apple does not remotely establish a likelihood of success on the merits, and the district court did not abuse its discretion in so holding.

II. The Equities Weigh Decisively Against Injunctive Relief.

A. The Balance Of Hardships Favors Defendants.

The balance of hardships weighs heavily against injunctive relief. As this Court already recognized, Teva would be harmed irreparably if this Court allows other applicants to enter the market during Teva's exclusivity period. *Teva*, 595 F.3d at 1311. Moreover, Teva would lose literally "hundreds of millions of dollars" from its competitors' entry into the market. *Id.* at 1314; *see also* A16 (an injunction "would certainly injure Teva").

By contrast, plaintiffs together stand to lose a combined maximum of $38.6 million if Teva maintains its exclusivity. A99; A49-50. As the district court properly recognized, those purely economic losses do not constitute irreparable harm under settled law. A16 (citing *Wisc. Gas*

Co. v. FERC, 758 F.2d 669, 674 (D.C. Cir. 1985); *Sociedad Anonima Viña Santa Rita v. Dep't of Treasury*, 193 F. Supp. 2d 6, 14 (D.D.C. 2001)). But even if they did, numerous courts have recognized that the kind of gross disparity in hardships at issue here weighs sharply against injunctive relief. *E.g.*, *Apotex v. FDA*, No. 06-0627, 2006 WL 1030151, *17-*18 (D.D.C. Apr. 19, 2006) ("In light of the considerable economic injury facing intervenor-defendants, and the less substantial injury to Apotex, the balance of hardships clearly tips against granting … emergency injunctive relief."); *see also Davis*, 571 F.3d at 1296 (Kavanaugh and Henderson, JJ., concurring); *Am. Ass'n for Homecare v. Leavitt*, No. 08-0992, 2008 WL 2580217, *4 (D.D.C. June 30, 2008).

Moreover, numerous courts addressing these issues under Hatch-Waxman have noted that the first applicant loses something far more important than money in these circumstances: "[U]nlike the harm that Apotex allegedly faces, the potential injury that [Teva faces] is not 'merely economic.' Rather, [Teva] stand[s] to lose a statutory entitlement, which is a harm that has been recognized as sufficiently irreparable. Once the statutory entitlement has been lost, it cannot be recaptured." *Apotex*, 2006 WL 1030151, *17; *Teva*, 595 F.3d at 1310,

1311 (noting that "Teva faces … a near-certain loss of the first-mover advantage," and that that loss cannot be recovered once other generics launch); *Mova*, 140 F.3d at 1066-67 n.6 (same); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 30-31 (D.D.C. 2006) (same).

Accordingly, the district court did not remotely (much less clearly) err when it found as a factual matter that the balance of hardships decisively weighs against injunctive relief.

B. The Public Interest Favors Defendants.

Whatever the balance of hardships between the parties, however, the public stands to lose the most if this Court enters an injunction that effectively—and irremediably—strips Teva of its exclusivity. While plaintiffs argue that the public stands to benefit because an injunction will "quickly … result in increased competition and reduced prices," Br. 35, their argument is squarely foreclosed by *Teva*:

> The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device [which] deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by the promise of a reward for generics that stick out their necks (at the potential cost of a patent infringement suit) by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted. As

> Congress deliberately created the 180-day exclusivity bonus, [plaintiffs] cannot justify [their claim to relief] by proudly proclaiming that [the public interest favors] eviscerate[ing] that bonus.

Id. at 1318. In short, as the district court recognized, irreparably divesting Teva of its exclusivity would thoroughly undercut the engine that drives challenges to competition-blocking patents, in direct contravention of Hatch-Waxman's "pro-consumer" goals. A16-17.

CONCLUSION

For the foregoing reasons, the district court's decision should be affirmed.

May 18, 2010

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 32(a)(7)(C); in accordance with this Court's April 21, 2010 briefing order granting appellees "14,000 words, to be divided among the two briefs as appellees see fit"; and consistent with the appellees' subsequent agreement to divide that word limit evenly, I hereby certify that this brief (excluding those portions exempted by the Rules) consists of 6,901 words.

May 18, 2010

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CERTIFICATE OF SERVICE

I hereby certify that on May 18, 2010, I caused the foregoing Brief to be served upon all counsel of record via this Court's CM/ECF system and overnight Federal Express delivery.

May 18, 2010

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