Appeal Nos. 2018-1976, 2018-2023

In the United States Court of Appeals for the Federal Circuit

GLAXOSMITHKLINE LLC, SMITHKLINE BEECHAM (CORK) LIMITED,

Plaintiffs – Appellants,

v.

TEVA PHARMACEUTICALS USA, INC.,

Defendant – Cross-Appellant.

Appeal from the United States District Court
for the District of Delaware in Case No. 14-cv-878-LPS-CJB,
Chief District Judge Leonard P. Stark.

BRIEF OF *AMICUS CURIAE* APOTEX INC. IN SUPPORT OF DEFENDANT – CROSS-APPELLANT'S PETITION FOR REHEARING EN BANC

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 18-1976, 18-2023

Short Case Caption GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.

Filing Party/Entity Apotex Inc.

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 12/15/2020

Signature: /s/Andrew M. Alul

Name: Andrew M. Alul

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Apotex Inc.		Apotex Pharmaceutical Holdings Inc.

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☑ None/Not Applicable ☐ Additional pages attached

5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

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6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

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TABLE OF ABBREVIATIONS

’000 patent	U.S. Patent No. RE40,000 (Appx31-45)
ANDA	Abbreviated New Drug Application pursuant to 21 U.S.C. § 355(j)
Apotex	*Amicus curiae* Apotex Inc.
CHF	Congestive heart failure
FDA	U.S. Food and Drug Administration
GSK	Plaintiffs-Appellants GlaxoSmithKline LLC and SmithKline Beecham (Cork) Limited
Hatch-Waxman or the Hatch-Waxman Act	Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at, *inter alia*, 21 U.S.C. § 355), as amended by the Medicare Prescription Drug, Improvement and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003)
Appx	Joint Appendix
Section viii statement	Statement pursuant to 21 U.S.C. § 355(j)(2)(A)(viii)
Teva	Defendant-Cross-Appellant Teva Pharmaceuticals USA, Inc.

INTEREST OF THE *AMICUS CURIAE*

Amicus curiae Apotex Inc. ("Apotex")[1] is a global generic drug company that frequently files ANDAs seeking approval from the FDA to market its drugs, and frequently "carves out" from its drug labels indications covered by patents that Apotex is not seeking FDA approval for, and submits with its ANDAs Section viii statements for those patents. In the last fifteen (15) years, Apotex has filed approximately thirty-nine (39) ANDAs with carve outs and Section viii statements, with at least 13 of those currently pending. Annually, in the United States, Apotex is engaged in dozens of patent lawsuits under the Hatch-Waxman Act.

Apotex has a significant interest in issues central to Teva's Petition for Rehearing En Banc (ECF No. 116). Congress intended for generic drug manufacturers to avoid infringement liability for method patents that claim uses the generic is not seeking FDA approval for. 21 U.S.C. § 355(j)(2)(A)(viii). Furthermore, years of jurisprudence from the Supreme Court and this Court have made clear that liability for induced infringement of a method patent under 35 U.S.C. § 271(b) requires an accused infringer to "encourage[], recommend[], or promote[]" the claimed method. *Grunenthal GmbH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1339

[1] Pursuant to Fed. R. App. P. 29(b)(3) and Federal Circuit Rule 35(g), Apotex files contemporaneously herewith its unopposed motion for leave to file this *amicus* brief. No counsel for any party authored this brief in any part, and no party, counsel, or person other than Apotex and its counsel contributed money to fund the preparation and submission of this brief. FED. R. APP. P. 29(a)(4)(E).

(Fed. Cir. 2019) (citing *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015)). As explained below, the panel decision in *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*, 976 F.3d 1347 (Fed. Cir. 2020) ("*GSK*") conflicts with Hatch-Waxman and years of precedent by finding that Teva induced infringement of the '000 patent during the skinny label phase of Teva's commercial marketing of its carvedilol ANDA product (September 2007 - April 2011 (Appx6-7)[2]), where there was a complete absence of evidence that Teva ever actually encouraged, instructed, or promoted direct infringement of the methods claimed in the '000 patent.

The ramifications for the generic drug industry and consumers are enormous—many generic drug companies, like Apotex, may now forgo filing ANDAs for off-patent drugs that carve out patented indications and only seek approval for off-patent uses. This is simply not what Congress intended, *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1359-62 (Fed. Cir. 2003), and will drastically undercut the goal of Hatch-Waxman: "to speed the introduction of low-cost generic drugs to market." *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670, 1676 (2012). Generic drug manufacturers like Apotex who routinely file ANDAs with Section viii statements and carve out patented uses from their drug

[2] All "Appx__" citations are to 18-1976 ECF Nos. 88-1 and 88-2, Corrected Non-Confidential Joint Appendix Volume Nos. I and II.

labels need clarity from this Court on how to reconcile *GSK* with § 355(j)(2)(A)(viii) and decisions of this Court that *GSK* directly conflicts with.

ARGUMENT

I. THE PANEL'S DECISION IS IN DIRECT CONFLICT WITH HATCH-WAXMAN AND PATENT INDUCEMENT CASE LAW

As this Court made clear in *Warner-Lambert* and *AstraZeneca Pharmaceuticals LP v. Apotex Corp.*, 669 F.3d 1370 (Fed. Cir. 2012), "an ANDA seeking to market a drug not covered by a composition patent for unpatented methods of treatment cannot infringe under [35 U.S.C.] § 271(e)(2)." *AstraZeneca*, 669 F.3d at 1379 (extending *Warner-Lambert*'s holding from patents claiming unapproved uses to those claiming approved uses the ANDA-filer is not seeking approval for); *see also Warner-Lambert*, 316 F.3d at 1363-66 (reaching the same conclusion under 35 U.S.C. § 271(b), even assuming as true that "Apotex expects to get an 'A-B rating' for its [product]"). Yet the *GSK* panel held the exact opposite: a generic drug company marketing an off-patent drug for unpatented uses can be liable for inducing infringement of a patent that the generic submitted a Section viii statement for and that covers a method that the generic carved out of its label. Apotex respectfully submits that the *GSK* panel's finding of substantial evidence supporting the jury's verdict of induced infringement during the skinny label phase is simply irreconcilable with 21 U.S.C. § 355(j)(2)(A)(viii) and this Court's decisions in *Warner-Lambert* and *AstraZeneca* interpreting and applying that

statute.

Section 355(j)(2)(A)(viii) considerations aside, the panel's decision conflicts with decades of Federal case law on induced infringement. "To prove inducement, a plaintiff must present evidence of active steps taken to encourage direct infringement; mere knowledge about a product's characteristics or that it may be put to infringing uses is not enough." *HZNP Meds. LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 701 (Fed. Cir. 2019) (citing *Takeda*, 785 F.3d at 630-31). Below is a summary of what the *GSK* panel relied on to support its substantial evidence finding during the skinny label phase (September 2007 - April 2011 (Appx6-7)):

Evidence	**Encourages, Recommends, or Promotes Infringement?**
1. June 9, 2004 Teva Press Release (Appx6347). *GSK*, 976 F.3d at 1353.	No. While this press release—which predates the '000 patent (January 8, 2008, Appx32) and Teva's carve out (August 2007, Appx5)—states that Teva's ANDA product is "indicated for treatment of heart failure and hypertension" (Appx6347), no mention of decreasing mortality or the actual claimed method.
2. August 2007 Teva's Prescribing Information (Appx5508). *GSK*, 976 F.3d at 1350, 1354-55.	No. Teva carved out the claimed indication.
3. September 6, 2007 Teva Press Release (Appx6353). *GSK*, 976 F.3d at 1353.	No. There is absolutely no mention of decreasing mortality or CHF, let alone the actual claimed method.
4. Spring 2008 Teva Product Catalog	No. There is absolutely no mention of

Evidence	Encourages, Recommends, or Promotes Infringement?
(Appx6221). *GSK*, 976 F.3d at 1353.	decreasing mortality or CHF, let alone the actual claimed method.
5. 2011 Teva Product Catalog (Appx6072). *GSK*, 976 F.3d at 1353.	No. There is absolutely no mention of decreasing mortality or CHF, let alone the actual claimed method.
6. Trial testimony of Teva's Rule 30(b)(6) witnesses, Director of New Products, Jennifer King. *GSK*, 976 F.3d at 1354.	No. The testimony relied on here only reflects that, even with the CHF carve out, "Teva still expects to get sales where the doctor prescribed carvedilol for [CHF]." *GSK*, 976 F.3d at 1354.
7. Trial Testimony of GSK's cardiologist, Dr. Peter McCullough. *GSK*, 976 F.3d at 1353-54.	No. The testimony relied on here only reflects that, based on Teva's June 9, 2004 Press Release (Appx6347), September 6, 2007 Press Release (Appx6353), and Teva's Spring 2008 Product Catalog (Appx6211), that Teva was expecting to receive, and did receive in 2007, an "AB-rating" for its carvedilol ANDA product, and that the "AB-rating" would "lead a doctor to believe that 'they're therapeutically interchangeable.'" *GSK*, 976 F.3d at 1354 (quoting Appx10634-45, Appx11659).

As can be seen, nothing in the documentary evidence (Nos. 1-5) that the *GSK* panel relied upon to assess the skinny label phase rises to the level of "encourage[ment], recommend[ation], or promot[ion]" of the claimed method heretofore required by this Court for a finding of induced infringement. *Grunenthal*, 919 F.3d at 1339. At best, the documents identified above describe Teva's ANDA

product as "AB-rated" to GSK's Coreg®—but, as the *GSK* panel recognized, the "AB-rating" only signifies a therapeutic equivalency evaluation by FDA, *GSK*, 976 F.3d at 1350 n.3, and says nothing about how Teva's carvedilol ANDA product should be used. Indeed, as FDA notes in the preface to the Orange Book, "[t]here may be labeling differences among pharmaceutically equivalent products that require attention on the part of the health professional . . . FDA's determination that such products are therapeutically equivalent is applicable only when each product is reconstituted, stored, and used under the conditions specified in its labeling." U.S Food and Drug Admin., *Approved Drug Products with Therapeutic Equivalence Evaluations* (40th Ed. 2020), Preface at xiv. Of course, Teva's ANDA product was ***not*** approved for treatment of CHF during the skinny label phase; thus, under FDA's own explanation of its therapeutic equivalence evaluation codes, an "AB-rating" for Teva's ANDA product during the skinny label phase did ***not*** mean that it was therapeutically equivalent to Coreg® with respect to treatment for CHF, or that it could be used for that indication. Moreover, most generic drugs are AB-rated; thus the panel's decision puts almost all generic versions of off-patent drugs approved for unpatented uses at risk.

The only other statement the *GSK* panel could point to in the documentary evidence to support its substantial evidence finding of inducement during the skinny label phase was the mention in Teva's 2004 Press Release that Teva's ANDA

product was "indicated for treatment of heart failure and hypertension." Appx6347; *GSK*, 976 F.3d at 1349, 1353-54. Even if this statement[3] is considered at face value, it cannot be probative of specific intent to induce infringement because it says nothing about the method actually claimed in the '000 patent.

For instance, there is no mention in the 2004 Teva Press Release (or in any of the other documentary evidence relied upon during the skinny label phase) of co-administration with "an angiotensin converting enzyme inhibitor (ACE), a diuretic, [or] digoxin," or administration of "daily maintenance dosages for a . . . period . . . greater than six months," as required by the '000 patent claims. Appx45. The panel's reliance on these documents—which do not even mention, let alone promote, the actual claimed method—to support a substantial evidence finding during the skinny label phase directly conflicts with decisions such as *Takeda*, 785 F.3d at 632 (post-approval in the § 271(b) context, no inducement where label did not instruct the claimed method (treatment of acute gout flares), and where the Court had to look beyond the label to "how physicians may act to find inducement"); *Grunenthal*, 919 F.3d at 1339-40 (no inducement of claims directed to treatment of polyneuropathic pain, were accused labels instructed for treatment moderate/severe chronic pain, which included polyneuropathic pain); and *HZNP*, 904 F.3d at 699-702 (no

[3] Apotex notes that there does not appear to be any evidence in the record suggesting that the 2004 Teva Press Release was publicly available during the life of the '000 patent.

inducement where accused label permitted, but did not require, direct infringement). Simply put, nothing in the documentary evidence that the panel relied upon during the skinny label phase could reasonably be read as an encouragement, recommendation, or promotion to use Teva's ANDA product to carry out the actual method claimed in the '000 patent.

The testimonial evidence the *GSK* panel relied upon to find substantial evidence of inducement fares no better. That GSK was able to produce an expert at trial who testified that health care providers reviewing Teva's Jun 9, 2004 and September 6, 2007 press releases and Spring 2008 Product Catalog would understand the statements therein to mean "'that we should be able to prescribe generic carvedilol for heart failure,'" and that the "AB-rating" would "lead a doctor to believe that 'they're therapeutically interchangeable.'" *GSK*, 976 F.3d at 1354 (quoting Appx10635-45, Appx11659), says nothing about whether Teva was actually "encourage[ing], recommend[ing], or promot[ing] infringement" of actual methods claimed in the '008 patent. *Grunenthal*, 919 F.3d at 1339; *see also Takeda*, 785 F.3d at 631 ("The question is not just whether instructions describe the infringing mode, . . . , but whether the instructions teach an infringing use of the devise *such that* we are willing to infer from those instructions and affirmative intent to infringe the patent." (internal quotations, citations, and brackets omitted) (emphasis in original)).

Moreover, this Court has rejected the relevance of such evidence in assessing inducement claims in the pharmaceutical context. In *AstraZeneca*, the brand argued that "Section viii statements and restricted generic labeling ignore market realities because even if a generic drug is formally approved only for unpatented uses, pharmacists and doctors will nonetheless substitute the generic for all indications once it becomes available." *AstraZeneca*, 669 F.3d at 1380. This Court expressly rejected the argument:

> First, AstraZeneca's position would, in practice, vitiate § 355(j)(2)(A)(viii) by enabling § 271(e)(2) infringement claims despite the fact that Appellees' Section viii statements and corresponding proposed labeling explicitly and undisputedly carve out all patented indications . . . . Moreover, if accepted, these speculative arguments would allow a pioneer drug manufacturer to maintain de facto indefinite exclusivity over a pharmaceutical compound by obtaining serial patents for approved methods of using the compound and then wielding § 271(e)(2) 'as a sword against any competitor's ANDA seeking approval to market an off-patent drug for an approved use not covered by the patent. Generic manufacturers would effectively be barred altogether from entering the market.' *Warner–Lambert*, 316 F.3d at 1359. We cannot agree with this expansive view of § 271(e)(2), which is contrary to the statutory scheme. If an off-patent drug is being used for an unpatented use, that is activity beyond the scope of § 271(a). So is filing an ANDA seeking to market an unpatented drug for an unpatented use beyond the scope of § 271(e)(2).

Id. at 1380. There is simply no way to reconcile the *GSK* panel's finding of sufficient evidence to support the jury's inducement verdict during the skinny label phase with *Warner-Lambert*, *AstraZeneca*, *Takeda*, *Grunenthal*, or *HZNP*.

II. *GSK* WILL BE POTENTIALLY DEVASTATING TO THE GENERIC INDUSTRY

Left uncorrected, the skinny label portion of *GSK* arguably does what this Court presciently warned about in *Warner-Lambert* and *AstraZeneca*: potentially allow brand drug companies to "maintain de facto indefinite exclusivity over a pharmaceutical compound by obtaining serial patents for approved methods of using the compound and then wielding § 271(e)(2) 'as a sword against any competitor's ANDA seeking approval to market an off-patent drug for an approved use not covered by the patent.'" *AstraZeneca*, 669 F.3d at 1380 (quoting *Warner–Lambert*, 316 F.3d at 1359). This is simply not what Congress intended with Hatch-Waxman, as "the statute was designed to enable the sale of drugs for non-patented uses even though this would result in some off-label infringing uses." *Takeda*, 785 F.3d at 631. Apotex and other generic companies will now likely curtail efforts to file ANDAs for unpatented uses of off-patent drugs, eliminating generic competition for many drugs with the end result being higher prescription drug prices for consumers. *GSK* entirely dis-incentivizes Apotex and other generics from utilizing Section viii statements; instead, Apotex and other generics will have every reason to file Paragraph IV certifications for patents covering uses the generic is not seeking approval for, resulting in 30-month stays that Congress never intended and further delaying generic competition. Apotex respectfully requests that this Court grant Teva's petition for rehearing en banc to correct at least the skinny label portion of

GSK.

Respectfully submitted,

Dated: December 15, 2020

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FORM 19. Certificate of Compliance with Type-Volume Limitations **Form 19**
July 2020

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

Case Number: 18-1976, 18-2023

Short Case Caption: GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.

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