No. 2023-1169

United States Court of Appeals for the Federal Circuit

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD.,

Plaintiffs-Appellants,

v.

HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC,

Defendants-Appellees,

HEALTH NET LLC,

Defendant.

Appeal from the United States District Court for the District of Delaware, Case No. 1:20-cv-01630-RGA-JLH, Judge Richard G. Andrews

BRIEF OF TEVA PHARMACEUTICALS USA, INC. AS AMICUS CURIAE IN SUPPORT OF APPELLEES

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September 5, 2024

CERTIFICATE OF INTEREST

Counsel for Amicus Curiae certifies the following:

1. **Represented Entities.** Provide the full names of all entities represented by undersigned counsel in this case. Fed. Cir. R. 47.4(a)(1).

   Teva Pharmaceuticals USA, Inc.

2. **Real Party in Interest.** 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. Fed. Cir. R. 47.4(a)(2).

   None

3. **Parent Corporations and Stockholders.** 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. Fed. Cir. R. 47.4(a)(3).

   Teva Pharmaceutical Industries, Ltd.

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

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).

   GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc., No. 14-878-LPS-CJB (D. Del.).

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).

   Not applicable

Dated: September 5, 2024

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INTRODUCTION AND INTEREST OF AMICUS CURIAE[1]

Teva Pharmaceuticals USA, Inc. is a leading manufacturer of both branded and generic drugs that has a strong interest in a clear and predictably functioning system for bringing new branded *and* generic drugs to market.

Teva has used and wishes to continue using Hatch-Waxman's section viii pathway to launch generic versions of off-patent drugs that have both patented and unpatented uses. Given its history with this Court's recent skinny-label jurisprudence, *see GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 25 F.4th 949 (Fed. Cir. 2022) (concurrence and three dissents in denial of rehearing en banc) (*GSK III*); *GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 7 F.4th 1320 (Fed. Cir. 2021) (*GSK II*); *GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 976 F.3d 1347 (Fed. Cir. 2020) (*GSK I*), *panel reh'g granted sua sponte, opinion withdrawn* (Feb. 9, 2021) (collectively, *GSK v. Teva*), Teva understands well the harmful unpredictability these decisions have created.

The Court has converted what have long been understood as "safe" launches of generic drugs—launches that avoid the risk of patent-infringement liability—into "at risk" launches that can expose generic manufacturers to hundreds of millions of dollars in damages. And the reasoning in both this case and *GSK II* demonstrates

[1] No party's counsel authored the brief in whole or in part, and no one other than *amicus* paid to prepare or submit the brief.

that there is nothing generic manufacturers can do to avoid this risk—Hatch-Waxman has no mechanism for pre-launch litigation involving skinny-labeled drugs, and the supposed indicia of active inducement both decisions mistakenly relied on will be present in virtually every skinny-label launch.

The shift in this Court's interpretation of the inducement statute, 35 U.S.C. § 271(b), and the skinny-label statute, 21 U.S.C. § 355(j)(2)(A)(viii), will prevent life-saving, low-cost generic drugs from reaching the market—to the detriment of patients and government payors. As the Solicitor General has explained and Teva knows first-hand, "[u]ncertainty about the section viii pathway is likely to deter generic manufacturers from invoking that mechanism, thereby threatening the availability of lower-cost generic drugs, in contravention of the statutory design." U.S. Amicus Br. 13, *Teva Pharm. USA, Inc. v. GlaxoSmithKline LLC*, Supreme Court No. 22-37 ("U.S. Br.").[2] This Court should grant rehearing en banc and reconsider its failed skinny-label experiment.

ARGUMENT

I. Skinny labels are one of Hatch-Waxman's three pathways for generic drugs to launch without risking large damages awards.

The Hatch-Waxman Act was adopted four decades ago as a "compromise" designed to bring generic drugs to market as early as possible. *Warner-Lambert Co.*

[2] https://tinyurl.com/p6mvfjcp.

v. Apotex Corp., 316 F.3d 1348, 1358 (Fed. Cir. 2003) (citing H.R. Rep. No. 98-857(I), at 14-15 (1984)). Branded manufacturers received regulatory exclusivities and a patent-term extension, while generic manufacturers were authorized to rely on research submitted by the brands, thereby eliminating the need to conduct the same safety and efficacy studies again. Cong. Res. Serv., *The Hatch-Waxman Act: A Primer* 5-6 (Sept. 28, 2016), https://tinyurl.com/jzzzfrnz.

The compromise included a process to address patent-infringement issues before generic launch. This allowed branded manufacturers to protect their market share without the need for frenzied preliminary-injunction proceedings, and it provided generic manufacturers with "patent certainty" so they could launch without risking massive lost-profits damages. *See Teva Pharm. USA, Inc. v. Novartis Pharm. Corp.*, 482 F.3d 1330, 1343-1344 (Fed. Cir. 2007) (quoting 149 Cong. Rec. S15885 (Nov. 25, 2003)). Hatch-Waxman balanced these interests by allowing brands to publicly list in the "Orange Book" patents that could be asserted against generic manufacturers, and establishing three pathways for generic manufacturers to launch after reviewing the Orange Book listing. First, generic manufacturers can wait until any listed patents expire. 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(III). Second, they can file a "paragraph IV" certification stating that the brand's patents are invalid or will not be infringed—this affirmatively provokes litigation, along with a 30-month stay on FDA approval, to resolve patent disputes *before* launch. *Id.*

§ 355(j)(2)(A)(vii)(IV); *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 407 (2012). Third, where patents on the branded *product* have expired and only *some* FDA-approved methods-of-use remain patented, they can seek approval for unpatented methods-of-use and "carve out" patented indications from the generic labeling. 21 U.S.C. § 355(j)(2)(A)(viii).

Section viii was created so "that one patented use will not foreclose marketing a generic drug for other unpatented ones," *Caraco*, 566 U.S. at 415, and to prevent brands from maintaining "de facto indefinite exclusivity" by procuring myriad method patents on off-patent drugs. *Astra-Zeneca Pharm. LP v. Apotex Corp.*, 669 F.3d 1370, 1380 (Fed. Cir. 2012). Congress understood that this pathway might lead to some off-label infringing uses because state law directs pharmacies to substitute generics without regard to the patient's intended use of the drug. *See Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631, 633 (Fed. Cir. 2015). Congress nonetheless decided to "enable the sale of drugs for non-patented uses even though" some infringing sales would naturally occur. *Id.* at 631. Congress understood that the inducement statute requires "inducing acts," *i.e.*, affirmative encouragement, by the alleged infringer, and launching with a *carved-out* label is not affirmative encouragement, even if an alleged infringer might have "knowledge of off-label infringing uses." *Id.* at 631-32. Thus, through section viii, Congress permitted generics to avoid the risk of lost-profits damages *and* the need for pre-

launch litigation.

II. This Court's recent skinny-label cases make section viii unusable by turning every section viii launch into an at-risk launch.

Congress's innovative system worked for decades—generics were largely able to avoid at-risk launches,[3] and if they carved out patented indications, they could predictably launch without the need for pre-launch litigation *or* the fear of a future lawsuit claiming hundreds of millions in damages. But that all changed with this Court's decisions in *GSK v. Teva* and this case, which allow brands to sue generics years after launching with a skinny-label that omits patented indications listed in the Orange Book, claiming that the skinny-label was not skinny enough or that doctors might construe standard and accurate characterizations of generic *products* as instructions to infringe omitted *methods-of-use*.

To be sure, the panel here and majority in *GSK v. Teva* attempted to downplay both decisions as case-specific. *GSK II*, 7 F.4th at 1326; Op. 16-18. But one should not be fooled. As Judge Prost noted (along with the Solicitor General, PTO, HHS, and FDA), there was nothing unique about the facts in *GSK v. Teva*. *GSK II*, 7 F.4th at 1360; U.S. Br. 22-23. The facts here are not unique either. Under this Court's erroneous new standard, there will always be *something* a brand can use to manufacture a factual dispute that will get past a motion to dismiss, summary

[3] Generics sometimes must still consider at-risk launch—*e.g.*, during an appeal after winning in district court—but much more rarely than before Hatch-Waxman.

judgment, and JMOL.

Cobbled-together label language—Both decisions deemed language on a skinny-label that did not *instruct* the carved-out patented indication, but simply bore some tangential relationship to that indication's patented elements, to be evidence of inducement. Here, for example, Hikma carved out the "CV" (cardiovascular) indication. But for the "SH" (severe hypertriglyceridemia) indication, the generic label said that certain SH patients who have a *risk factor for* cardiovascular disease may experience heart-rhythm problems as a side effect. Op. 43. The Court accepted that physicians might read this language, combined with other statements, as an instruction to prescribe the drug *to reduce cardiovascular risk*. Op. 15-17.

In *GSK v. Teva*, Teva carved out 50 paragraphs pertaining to the narrow patented "CHF" indication: using carvedilol for 6+ months with an ACE inhibitor, diuretic, or digoxin to reduce mortality caused by symptomatic congestive heart failure. The majority took language from disparate portions of the skinny-label obliquely referencing some claim elements—a reference to patients "with *or without* symptomatic heart failure" here, a note that *some* clinical-trial patients who took the drug after a heart attack had also been taking ACE inhibitors or diuretics there—and concluded that physicians might combine those references and think Teva was *encouraging* them to use the carved-out method. *GSK II*, 7 F.4th at 1328-1331.

That mode of analysis eviscerates inducement's active-encouragement

requirement—which, in the context of off-patent products with both patented and unpatented uses, is critical. It "overcomes the law's reluctance to find liability when a defendant merely sells a commercial product suitable for some lawful use." *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005). This Court had previously agreed, forbidding liability in carve-out cases based on arguments that "vague label language" plus "[s]peculation or even proof that some, or even many, doctors would prescribe" the drug for an infringing use could constitute active encouragement. *Takeda*, 785 F.3d at 632-633. In essence, *GSK II* and this case adopted a series of *dissents* as the Circuit's new position. *Takeda*, 785 F.3d at 635-636 (Newman, J., dissenting); *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1329 (Fed. Cir. 2012) (Newman, J., dissenting); *HZNP Medicines LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 709 (Fed. Cir. 2019) (Newman, J., dissenting).

Virtually every skinny-label launch will involve these types of facts. When a drug is approved for multiple uses, those uses frequently bear some relationship to one another. *E.g.*, *Takeda*, 785 F.3d at 630 (unpatented gout-*prevention* indication and patented gout-*treatment* indication); *Abraxis Bioscience, Inc. v. Navinta LLC*, 625 F.3d 1359, 1362 (Fed. Cir. 2010) (patented and unpatented indications differing only by concentration level). Brands will always be able to find *something* in a carved-out label and claim that doctors could read it as encouraging an omitted use.

That perverse outcome is exacerbated by the fact that *brands* control drug

labeling; generics cannot change the language brands use for unpatented indications. U.S. Br. 18-19 ("A generic manufacturer … is not free to omit additional portions of the brand-name labeling beyond the [carve-out] omissions approved by FDA."); 21 C.F.R. § 314.127(a)(7) (FDA "will refuse to approve" an ANDA unless "the labeling proposed for the drug is the same"). Accordingly, these decisions will, as one FDA attorney noted, encourage brands to "seed potentially problematic language" in unpatented indications that could support future inducement liability. Ian Lopez, *Hikma Drug Label Win Still Leaves Generics on Hook for Liability*, Bloomberg Law (Jan. 12, 2022), https://tinyurl.com/43j7dfjh. In short, these decisions "invite[] gamesmanship by brand-name manufacturers." U.S. Br. 17.

General product references—In both cases, the court concluded that referring to generic products as the "generic version" or "generic equivalent" of the branded drug could constitute affirmative encouragement of a carved-out use. Op. 6, 17, 18, 19; *GSK II*, 7 F.4th at 1336, 1337. These statements should be irrelevant to inducement in the skinny-label context because they are references to the drug *product*. A skinny-label launch inherently means the drug *product* is no longer patented; only some methods-of-use are. So the inducement analysis should require statements actively encouraging the *patented method-of-use*.

Moreover, references to generic products as a "generic version" or "generic equivalent" will be present in nearly every skinny-label launch. Generic

manufacturers—plus Congress and FDA—commonly refer to generic drugs this way because they *are* "generic versions" or "generic equivalents" of branded drugs. *E.g.*, 21 U.S.C. § 353d(a)(1)(3) ("The term 'generic version' means a drug approved under section 355(j) … whose reference listed drug is a covered drug."). Indeed, generics are *required* to demonstrate bioequivalence to brands for FDA approval. 21 C.F.R. § 314.94(a)(7).[4]

References to brand revenues—The panel here also found indicia of inducement in press releases that referenced the branded drug's *total* sales revenue. Op. 6, 17, 18, 19. This, too, is standard for skinny-label launches because indication-by-indication revenues for brand-name drugs is the stuff of expert testimony at trial, not generic manufacturer business records. Moreover, press releases are issued to alert *investors* to developments that could impact the company's finances; they are not treatment instructions to physicians.[5]

[4] The panel here also faulted Hikma for calling its drug the "generic version" without always noting its "AB rating," suggesting that physicians might read the lack of an AB-rating notation as encouragement to prescribe the drug for a carved-out indication. Op. 18. The panel in *GSK II* said the opposite—that *including* "AB rated representations" was "affirmative evidence" of inducement. 7 F.4th at 1335. More proof that every case will get to a jury.

[5] Both decisions also mistakenly view press releases, product listings, etc. as "marketing"—*i.e.*, advertising—to physicians. Op. 7, 13, 18; *GSK II*, 7 F.4th at 1338. But generics do not typically advertise to doctors or patients—not just because profit margins are thin, but also because pharmacy-substitution practices make advertising a colossal waste of money: physicians cannot prescribe *a particular manufacturer's* generic drug because pharmacies dispense whichever generic they have in stock.

In short, now that *every* skinny-label launch is an at-risk launch, the economics will rarely make sense, as the United States has recognized. U.S. Br. 13, 21. GSK, for example, sought nearly $750 million in lost profits—ten times Teva's total carvedilol revenues ($74.5 million, a $13 million net *loss*). *See GSK I*, 976 F.3d at 1363 n.3 (Prost, J., dissenting). If every skinny-label launch is an at-risk launch, "generics simply won't play." U.S. Br. 21 (citation omitted)).

The real losers will be the public. When a drug has patented and unpatented uses, the first generic launches with a skinny-label nearly half the time,[6] saving patients and the government billions. *See* U.S. Br. 20. With generics accounting for 90% of prescriptions but just 20% of prescription-drug costs, a properly functioning Hatch-Waxman regime—including the skinny-label statute—is crucial.[7]

III. This Court should reconsider its approach and harmonize the inducement and skinny-label statutes.

This Court should grant rehearing en banc and take the opportunity to completely revisit its recently changed approach to skinny-label inducement claims.

This Court's recent skinny-label jurisprudence makes using the carve-out untenable. There is *no mechanism* for generic manufacturers to obtain patent certainty before a skinny-label launch—Hatch-Waxman's carve-out provision was

[6] Bryan S. Walsh et al., *Frequency of First Generic Drug Approvals With 'Skinny Labels' in the United States*, 181 JAMA Intern. Med. 995-997 (2021).
[7] Association for Accessible Medicines, *The U.S. Generic & Biosimilar Medicines Savings Report* 7 (2023), https://tinyurl.com/8wbmczpj.

crafted to allow generics to *avoid litigation altogether*, rather than simply litigate *before launch*. That is why a skinny-label ANDA applicant need not notify the patent-holder of its carve-out decision, the 30-month stay does not apply, and filing the skinny-label ANDA is neither an act of infringement nor cause for immediate suit. *See AstraZeneca*, 669 F.3d at 1377-1378 (citing *Warner-Lambert*, 316 F.3d at 1356-1360). When generics have tried to obtain patent certainty before a skinny-label launch, brands have successfully defeated those claims by arguing that there is no statutory basis for them. *In re Entresto (Sacubitril/Valsartan) Patent Litig.*, 2022 WL 4482717, at *5 (D. Del. Sept. 27, 2022). This Court's decisions therefore make skinny-label launch the *riskiest* option.

The last time the Court considered whether to address this issue en banc, it did not have the benefit of the government's views. But the Solicitor General, FDA, PTO, and HHS have since weighed in. They have recognized that this Court's interpretation is at odds with the text and structure of the skinny-label and inducement statutes, with harmful ramifications for patients. U.S. Br. 13. Taking these views into account, this Court should revisit its skinny-label jurisprudence so "that one patented use will not foreclose marketing a generic drug for other un-patented ones." *Caraco*, 566 U.S. at 415.

CONCLUSION

This Court should grant rehearing en banc.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the length limitation set forth in Federal Circuit Rule 35(g)(3) because it contains 2,595 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f) and Federal Circuit Rule 32(b)(2).

This brief complies with the typeface requirements of Fed. R. App. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced typeface, 14-point Times New Roman, using Microsoft Word 365.

Dated: September 5, 2024

/s/ William M. Jay
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