No. 2023-1169

IN THE

United States Court of Appeals for the Federal Circuit

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LTD., 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, NO. 1:20-CV-1630, JUDGE RICHARD G. ANDREWS

BRIEF OF 15 SCHOLARS OF LAW AND MEDICINE AS *AMICI CURIAE* IN SUPPORT OF THE PETITION FOR REHEARING EN BANC

CHARLES DUAN
Counsel of Record
AMERICAN UNIVERSITY WASHINGTON COLLEGE OF LAW
4300 Nebraska Avenue NW
Washington, DC 20016
(202) 274-4124
notices.ecf@cduan.com

Counsel for Amici Curiae

CERTIFICATE OF INTEREST

Pursuant to Rules 29(a) and 47.4 of the Federal Circuit Rules of Practice, counsel certifies as follows:

(1) The full name of every party or amicus represented by me is **Michael Carrier, Thomas Cheng, Jonathan J. Darrow, Charles Duan, William Feldman, Aaron S. Kesselheim, Mark A. Lemley, Yvette Joy Liebesman, Lee Ann Wheelis Lockridge, Tyler Ochoa, Jordan Paradise, Joshua D. Sarnoff, Michael S. Sinha, S. Sean Tu, and Liza Vertinsky**.

(2) The above-identified parties are the real parties in interest.

(3) The corporate disclosure statement of Rule 26.1 of the Federal Rules of Appellate Procedure is as follows: There is no parent corporation to or any corporation that owns 10% or more of stock in the above-identified parties.

(4) The names of all law firms and the partners and associates that have appeared for the party in the lower tribunal or are expected to appear for the party in this court, not including those who have entered or are expected to enter an appearance before this court, are: **None**.

(5) The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal are: **None**.

(6) All information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees): **None**.

Although it is not required, S. Sean Tu and Jonathan Darrow wish to disclose that a portion of their research is funded by Arnold Ventures.

Dated: September 4, 2024

/s/ Charles Duan
Charles Duan
Counsel for Amici Curiae

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INTEREST OF *AMICI CURIAE*

Amici curiae[1] are scholars of law and medicine, listed in the Appendix. Their interest is in the proper development of patent law in ways that best promote the interests of innovation access and the public interest.

SUMMARY OF ARGUMENT

The panel decision announces an over-expansive, ill-defined doctrine of inducement, in which well-pled allegations may be based on nothing more than ordinary marketing materials and mandatory labeling—even when those materials never recite or describe the claimed invention. This unprecedented and erroneous expansion of inducement liability leaves the law uncertain. It is now unclear, among other things, what statements a generic firm may make about its own product's equivalence and how much of the generic product's labeling information must be revised—assuming that such revisions are even regulatorily allowed—in order to avoid the risk of an inducement lawsuit.

Absent clarification, the panel decision's unbounded inducement theories have the potential to harm competition in the pharmaceutical industry, to un-

[1]Pursuant to Federal Rule of Appellate Procedure 29(a), all parties received appropriate notice of and consented to the filing of this brief. Pursuant to Rule 29(c)(5), no counsel for a party authored this brief in whole or in part, and no person or entity, other than *amici*, their members, or their counsel, made a monetary contribution to the preparation or submission of this brief.

dermine federal policy encouraging "skinny labeling" and a robust generic drug market, to promote strategies of regulatory manipulation, and to confuse patients with misleading drug information. And because the inducement doctrine is not limited to pharmaceutical patents, the decision could have far-reaching effects on other industries and technological fields. En banc rehearing is warranted.

ARGUMENT

I. The Panel Decision's Erroneous Expansion of Inducement Renders the Doctrine Uncertain

The panel decision creates uncertainty for competitive generic drug manufacturers. Uncertainty is problematic in itself, and it is contrary to the legislative scheme for generic drugs. In situations like the present case, where the patents at issue cover not a drug compound itself but methods of using the drug to treat certain specific indications, Congress created the so-called "skinny labeling" pathway to enable introduction of competitive products approved for unpatented indications. *See* Federal Food, Drug, and Cosmetics Act (FFDCA) § 505(j)(2)(A)(viii), 21 U.S.C. § 355. This pathway was designed to provide certainty to generic manufacturers of drugs covered only by method-of-use patents.[2] Confusion over how to market generic drugs conflicts with this intended certainty.

[2] *See Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 415 (2012); *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 880 (D.C. Cir. 2004); Shashank Upadhye, *Generic Pharmaceutical Patent and FDA Law* § 26:11 (2020).

A. A Wide and Indeterminate Range of Generalized Marketing Statements May Now Suffice for a Plausible Inducement Case

First, the decision creates uncertainty about what allegations of inducement suffice to overcome a motion to dismiss, particularly when none of the alleged acts describe the infringing method of use. Generic firms are left to wonder what they can say about their products without triggering an inducement claim.

Amarin alleges inducement based on three pieces of information: Hikma's drug labeling, marketing statements mentioning generic equivalence and AB codes, and sales data. None, the panel agrees (at 15–17), identifies the patented indication of certain cardiovascular risks. Moreover, all three items are commonplaces of pharmaceutical marketing. Labeling is mandatory for approval of a generic drug by the U.S. Food and Drug Administration ("FDA"). *See* FFDCA § 505(j)(4)(G). That a generic drug is, in fact, a generic equivalent is not just an ordinary truthful statement, but again a mandatory requirement of generic drug approval. *See id.* § 505(j)(4)(F) (requiring "bioequivalence"). And sales data about a competitor is regular comparative advertising—products often tout themselves as "just as good as the leading brand." If common, generic marketing statements like these suffice for an inducement complaint, then it is all but impossible to tell what statements avoid risk.

The panel decision offers no clear theory or mechanism by which a doctor would be encouraged to use the patented method based on statements that say

nothing about the method. This omission is crucial. The unstated assumption is that an inducement case can rest on external knowledge and inferences about the specific method. What external knowledge and inferences are permissible for stating a claim for inducement, the panel does not say.

Even more puzzling is the panel decision's distinction (at 18–19) between "AB-rated" and "generic equivalent," suggesting the former term indicates "equivalence for only labeled uses." That distinction is questionable at best: Drugs of identical active ingredients, dosage forms, and routes of administration "generally will be coded AB if data and information are submitted demonstrating bioequivalence." Food & Drug Admin., *Approved Drug Products with Therapeutic Equivalence Evaluations* xv (44th ed. 2024) [hereinafter *Orange Book*]. Bioequivalence is based on "the rate and extent of absorption of the drug" into the body, irrespective of labeled uses. FFDCA § 505(j)(8)(B); 21 C.F.R. § 320.24.[3] This only adds uncertainty about what marketing language is allowed.

[3]The indication-agnostic nature of AB codes is unaffected by the FDA's definition of "therapeutic equivalents" as drugs "for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling." 21 C.F.R. § 314.3(b), *quoted in GlaxoSmithKline LLC v. Teva Pharms. USA*, 7 F.4th 1320, 1325 (Fed. Cir. 2021) (per curiam). The AB code is assigned based on bioequivalence evidence, not therapeutic equivalence. *See Orange Book*, *supra*, at xv. Even if the definition of "therapeutic equivalents" is relevant, the reference to "conditions specified in the labeling" appears to be merely prophetic ("can be expected"); the actual determination is based on indication-agnostic bioequivalence.

The panel decision turns the marketing of generics into a minefield, forcing generics to treat as risky even the most conventional marketing statements that do not describe the patented method.

B. The Decision Further Confuses the Question of Whether Mandatory Labeling Information Can Induce Infringement

Even greater uncertainty arises from the panel decision's expansion of the suggestion in *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA* that mandatory drug labeling can be sufficient to show inducement. There, the generic manufacturer carved out specific mentions of the infringing method of use, to the satisfaction of the FDA. *See* 7 F.4th 1320, 1324–25 (Fed. Cir. 2021) (per curiam). Nevertheless, *GlaxoSmithKline* permitted the patent holder to cobble together an inferential inducement theory, based on disparate parts of the labeling. *See id.* at 1328–29.

The panel decision here has arguably expanded this inducement-by-label theory. *GlaxoSmithKline* did not clearly hold that labeling alone could induce; there were also press releases involved. *See id.* at 1335. But here, the panel (at 19) characterized *GlaxoSmithKline* as a case in which "the generic manufacturer's label had unsuccessfully carved out the patented use," suggesting that the label standing alone might suffice to support an inducement claim.

This expanded inducement-by-label theory suggests that generic firms must carve out more language from labels. Otherwise, any stray statements could be cobbled together to make an inducement case that can survive a motion to dismiss—particularly if inducement can be premised on statements making no literal mention of the patented method.

Inducement by label is especially problematic because the generic firm does not write its own label—the patent holder writes it. A generic drug's labeling must statutorily be "the same as the labeling for" the original (patented) product. FFDCA § 505(j)(4)(G). Historically, the FDA has disallowed labeling changes to safety or dosage information, regardless of intellectual property concerns. *See AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1058–58 (Fed. Cir. 2010); *SmithKline Beecham Consumer Healthcare, LP v. Watson Pharms., Inc.*, 211 F.3d 21, 24 (2d Cir. 2000). Navigating an uncertain standard for what parts of labeling can trigger an inducement lawsuit is thus especially difficult in view of these regulatory requirements.

The panel decision thus expands the uncertainty, introduced by *GlaxoSmith-Kline*, about whether and what parts of mandatory labeling can serve as the basis for patent inducement.

II. Uncertainty About Inducement Resulting from This Decision Will Be Harmful

Although inducement law uncertainty is reason enough to grant rehearing, this uncertainty is especially harmful to competition, the regulatory system, and consumers.

These harms are contrary to the structure and purposes of pharmaceutical and patent law, which "is designed to speed the introduction of low-cost generic drugs," saving Americans millions of dollars each year and "do[ing] more to contain the cost of elderly care than perhaps anything else this Congress has passed."[4] Skinny labeling of drugs is a fixture of this structure, used for a wide range of generics.[5] It has saved Medicare Part D $15 billion and accelerated generic entry by an average of 2.5 years between 2015 and 2019, with similar benefits for biologic medicines.[6] Patent inducement law ought not undermine these beneficial objectives.

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[4] *Caraco*, 566 U.S. at 405; 130 Cong. Rec. 24427 (1984) (statement of Rep. Henry Waxman); *see also* Michael A. Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 Mich. L. Rev. 37, 42 (2009).

[5] *See* Bryan S. Walsh et al., *Frequency of First Generic Drug Approvals with "Skinny Labels" in the United States*, 181 JAMA Internal Med. 995, 997 (2021).

[6] *See* Alexander C. Egilman et al., *Estimated Medicare Part D Savings from Generic Drugs with a Skinny Label*, 177 Annals Internal Med. 833 (2024); Alexander C. Egilman et al., *Frequency of Approval and Marketing of Biosimilars with a Skinny Label and Associated Medicare Savings*, 183 JAMA Internal Med. 82 (2023).

A. It Will Stymie Competition

The vague expansion of inducement liability will be a powerful tool for hampering competition. Because a method of using a drug is not necessarily unpatentable over the drug itself, method-of-use patents can be obtained serially without end, each sufficient to block generic competitors based on generic statements of equivalence. *See* S. Sean Tu & Aaron S. Kesselheim, *Preserving Timely Generic Drug Competition with Legislation on "Skinny Labeling,"* 115 Clinical Pharmacology & Therapeutics 22 (2024); S. Sean Tu & Charles Duan, *Pharmaceutical Patent Two-Step: The Adverse Advent of Amarin v. Hikma Type Litigation*, 12 N.Y.U. J. Intell. Prop. & Ent. L. 1, 14 (2022). Indeed, the number of method-of-use patents appears to be increasing. *See* S. Sean Tu & Ameet Sarpatwari, *A "Method of Use" to Prevent Generic and Biosimilar Entry*, 388 New Eng. J. Med. 483, 485 & fig. (2023). To be sure, the panel decision relates only to initial allegations on a motion to dismiss, but the risks and costs of inducement litigation would likely be enough to dissuade a great deal of generic competition.

To be sure, innovation to develop new methods of using drugs is desirable. Insofar as off-label use of drugs makes enforcement of method-of-use patents difficult, however, that is a policy choice that Congress made in permitting off-label uses of prescription drugs; it is up to Congress to address that. Expanding inducement law as the panel decision did here, however, is unlikely to create

the right innovation incentives, because it will tend to reward marginal, narrow tweaks over major improvements. *See* Charles Duan, *Mandatory Infringement*, 75 Fla. L. Rev. 219, 255–58 (2023).

B. It Will Invite Regulatory Manipulation

The panel decision also invites manipulation of the drug regulatory system. The conduct that the panel relies on to support an inducement complaint—labeling, press releases, and generic equivalence—are not free-market choices for which Hikma voluntarily accepted risks, but rather are tightly regulated. *See* FFDCA § 505(j)(4)(F)–(G) (bioequivalence, same labeling); 21 C.F.R. § 202.1(*l*) (advertisements within scope of labeling).

Overlap between the regulatory and patent systems invites manipulation of the regulatory system to entangle competitors. *See generally* Duan, *supra*. As noted above, generic firms must use the same labeling text as their patented counterparts. *See* FFDCA § 505(j)(4)(G). So a method-of-use drug patent holder could write labeling information such that the infringing method could be inferred from the safety data, for example; the FDA would likely disallow removal of that information in the labeling of generic equivalents, setting up those generic firms for an inducement lawsuit through no choice of their own. *See* Duan, *supra*, at 236–40.

The expansion of patent inducement opens up a powerful new avenue for

manipulation, which turns the regulatory system into a weapon against competition, wastes government resources, and impedes the objectives of both patent and administrative law.

C. It Will Confuse Consumers

Ultimately, the harms flowing from an uncertain inducement standard fall upon American consumers. In part this is because of uncompetitive prices and diminished competition for drugs. But it is also because the panel decision creates liability risks for truthful, non-misleading factual advertising.

The panel decision (at 18–19) proposes that marketing statements including generic equivalence, perhaps cobbled together with inferences based on stray labeling statements, can induce patent infringement. The decision thus encourages generic firms (1) to excise more content from their labeling and/or (2) to describe their generic products as something other than generic equivalents.

Either action is harmful to patients. If generics must excise even more information to avoid inducement (assuming the FDA allows the omissions), then patients may not be presented with critical safety, dosage, or usage information from the label. Encouraging generics to omit important information for the sake of avoiding a hazy inducement allegation contravenes the very purpose of labeling—to protect and inform patients and their providers.

If generic firms must describe their generic products as something other than

generic equivalents, the natural implication for patients is that those generic products are *not equivalent*. The panel decision's phrase "AB-rated" is meaningless to ordinary non-lawyer patients. Consequent uncertainty and confusion could lead patients to be unnecessarily wary of generic drugs, contrary to federal policy that seeks to boost confidence in the substitutability of generics. *See* Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch–Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era?*, 15 Yale J. Health Pol'y L. & Ethics 293, 311–12 (2015).

Rehearing is warranted to avoid these harms, stemming from an improper expansion of patent inducement law.

III. Harms Resulting from Uncertainty About Inducement Law Extend Beyond the Generic Drug Industry

While this case has focused on pharmaceuticals, its doctrinal consequences reach potentially far beyond that industry. Statements of equivalence with other products are common in many different fields, and may now be caught unwittingly in a net of patent inducement.

Consider computer technology. Many products advertise themselves as compatible with technology standards—5G for mobile communications or H.264 for digital videos, among others. *See generally* Nat'l Acad. of Scis., *Patent Challenges for Standard-Setting in the Global Economy* 16 (Keith Maskus & Stephen A. Mer-

rill eds., 2013). Some patents cover the technologies in the standards themselves, such that products cannot be compatible without infringing those "standard-essential" patents; a complex system of law and contracts governs those patents. *See, e.g., Ericsson, Inc. v. D-Link Sys., Inc.*, 773 F.3d 1201, 1229–35 (Fed. Cir. 2014).

But there are also patents on methods of using a standard, say on using 5G communications for transmitting books or video. Such patents are not "essential" to using the standard. But if marketing a product as "equivalent" creates a plausible case for inducement of patent infringement, then the door is open to arguing that marketing a product as "compatible" induces infringement as well.

An insufficiently bounded inducement doctrine could thus invite a wide range of patent litigation well beyond pharmaceuticals. Such expansive implications are further reason to grant rehearing.

CONCLUSION

For the foregoing reasons, the Court should grant en banc rehearing.

Respectfully submitted,

Dated: September 4, 2024

/s/ Charles Duan

Charles Duan
Counsel of Record
American University Washington College of Law
4300 Nebraska Avenue NW
Washington, DC 20016
(202) 274-4124
notices.ecf@cduan.com

Counsel for Amici Curiae

APPENDIX
List of Academic Signatories

The brief presents the views of the individual signers. Institutions are listed for identification purposes only.

Michael Carrier

Rutgers Law School

Thomas Cheng

University of Hong Kong, Faculty of Law

Jonathan J. Darrow

Baylor College of Medicine

Charles Duan

American University Washington College of Law

William Feldman

Harvard Medical School

Aaron S. Kesselheim

Harvard Medical School

Mark A. Lemley

Stanford Law School

Yvette Joy Liebesman

Saint Louis University School of Law

Lee Ann Wheelis Lockridge

Louisiana State University Law Center

Tyler Ochoa

Santa Clara University School of Law

Jordan Paradise

Loyola University Chicago School of Law

Joshua D. Sarnoff

DePaul College of Law

Michael S. Sinha

Saint Louis University School of Law

S. Sean Tu

West Virginia University College of Law

Liza Vertinsky

University of Maryland Francis King Carey School of Law

CERTIFICATE OF COMPLIANCE

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Dated: September 4, 2024 */s/ Charles Duan*
Charles Duan
Counsel for Amici Curiae