No. 24-889

IN THE

Supreme Court of the United States

HIKMA PHARMACEUTICALS USA INC., et al.,

Petitioners,

v.

AMARIN PHARMA, INC., et al.,

Respondents.

ON WRIT OF CERTIORARI TO
THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

BRIEF FOR PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AND BIOTECHNOLOGY INNOVATION ORGANIZATION AS *AMICI CURIAE* IN SUPPORT OF RESPONDENTS

David E. Korn
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA
670 Maine Ave., SW
Washington, DC 20024
(202) 835-3400

Sarah E. Harrington
Counsel of Record
Michael N. Kennedy
Krista H. Carver
COVINGTON & BURLING LLP
850 Tenth Street, NW
Washington, DC 20001
(202) 662-6000
sharrington@cov.com

Counsel for Amici Curiae

Additional Counsel Listed on Inside Cover

Joseph B. Franklin
John T. Delacourt
BIOTECHNOLOGY
INNOVATION
ORGANIZATION
1201 New York Ave., NW
Washington, DC 20005

Charlotte S. Butash
COVINGTON & BURLING
LLP
30 Hudson Yards
New York, NY 10001

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INTEREST OF AMICI CURIAE[1]

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading innovative biopharmaceutical research companies, which are focused on developing innovative medicines that transform lives and create a healthier world. Together, PhRMA's member companies are fighting for solutions to ensure patients can access and afford medicines that prevent, treat, and cure disease. PhRMA member companies have invested more than $850 billion in the search for new treatments and cures over the last decade, supporting nearly five million jobs in the United States.

Biotechnology Innovation Organization (BIO) is the premier biotechnology advocacy organization representing biotech companies, industry leaders, and state biotech associations in the United States and more than 35 countries around the globe. BIO members range from biotech start-ups to some of the world's largest biopharmaceutical companies—all united by the same goal: to develop medical and scientific breakthroughs that prevent and fight disease, restore health, and improve patients' lives. Many of BIO's members are small companies that have yet to bring products to market or to attain profitability. These members rely heavily on venture capital and

[1] No counsel for a party authored this brief in whole or in part. No party, counsel for a party, or any person other than amici and their counsel made a monetary contribution intended to fund the preparation or submission of this brief.

other private investment, based on and protected by strong intellectual property rights.

Amici's members share a significant interest in the proper application of the framework Congress established in the Hatch-Waxman Act, 21 U.S.C. §§ 355, *et seq.*, which strikes a careful balance between permitting generic drugs to enter the market and promoting ongoing investment in much-needed post-approval research of approved, innovative medicines. Although amici's members recognize that a return on their substantial investments in pharmaceutical research and innovation is never guaranteed, the meaningful protections found in the U.S. patent system for both initial *and* subsequently approved drug indications justify those investments and encourage the cutting-edge drug innovation at the heart of this country's pharmaceutical industry.

INTRODUCTION AND SUMMARY

Research and clinical trials following a drug's initial approval are vital for medical progress, drug innovation, and public health. After a drug's initial approval by the Food and Drug Administration (FDA), it is not unusual for the drug's manufacturer to invest hundreds of millions of dollars to investigate and develop additional uses for that drug. Resulting FDA-approved indications provide new or improved treatment options for a variety of diseases and conditions, including hard-to-treat and rare diseases. And these medical advancements require massive investments—multi-year clinical programs and expensive outcomes trials that often exceed the effort behind the clinical program for the first approved use.

I. The Hatch-Waxman Act, 21 U.S.C. §§ 355, *et seq.*, represented Congress's solution to balancing its desire to expedite market entry for generic drugs with the need to preserve incentives for drug innovation, including in new uses of approved drugs. The Act does so by establishing an abbreviated FDA approval process that allows generic manufacturers to sell their products for unpatented uses. At the same time, the Act maintains meaningful protections for patented indications. This balance encourages the search for new drug indications through scientifically rigorous research and development after initial approval, while permitting generic manufacturers to enter the market where their generic drugs are labeled and promoted only for unpatented indications.

The Federal Circuit's decision in this case permitting Respondents' patent infringement inducement

suit to proceed past the motion-to-dismiss stage is a faithful implementation of that settled regulatory regime and long-established patent law. In asking this Court to affirm that decision, Respondents seek only the chance to prove their allegations that Petitioners induced infringement of Respondents' patent. Respondents do not seek special rules or expanded patent rights. They seek only application of ordinary inducement principles, under which courts—not generic manufacturers—determine whether conduct unlawfully encourages patented uses.

Petitioners in contrast ask this Court to upend Congress's careful design and award them a special immunity from inducement liability not afforded to companies in any other sector. But the bright-line, generic drug-specific immunity that Petitioners seek in the name of improving access to medicines for patients would actually result in a contrary outcome. It would erode drug innovation incentives, chill post-approval research, and ultimately deprive patients of new treatments—backed by clinical trials demonstrating each use's safety and efficacy—that will improve their lives. This Court should reject Petitioners' invitation to accord them special treatment. It should instead honor Congress's weighing of interests in the Hatch-Waxman Act and protect the ability of this country's pharmaceutical companies to develop innovative and transformative new treatments for patients who need them most.

II. The drug innovation at the core of this case is essential to public health. Medical progress depends on costly investment in research and development, including investments to study existing medicines for

potential new uses. That post-approval research has delivered important new treatments for hard-to-treat and rare diseases, and the benefits of some of these new uses have dwarfed the benefits of the original indication several times over. But medical breakthroughs take time, and they take money. Ruling in favor of Petitioners will undercut the incentives that drive innovation, and when innovation falters, American patients waiting on new pharmaceutical treatments suffer.

ARGUMENT

I. Petitioners Seek a Special Immunity for Generic Drugs That Has No Basis in the Hatch-Waxman Act.

Over forty years ago, Congress enacted the Drug Price Competition and Patent Term Restoration Act, better known as the Hatch-Waxman Act, 21 U.S.C. §§ 355, *et seq.*, to streamline the process for approving generic drugs while preserving incentives for innovation. On one side of the ledger, Congress created a new path for generic manufacturers to bring their drugs to market through an abbreviated pathway. One part of this pathway allows generic companies to seek approval only for non-patented uses of the innovator drug while "carving out" a patented use. On the other side of the ledger, Congress provided incentives to ensure that pharmaceutical companies would continue researching and developing new, innovative medicines—including new uses of approved drugs—by, among other things, preserving patent protection for such new uses and maintaining the applicability

of the Patent Act for any patent issues not resolved before a generic launch.

That balance has proven remarkably effective at achieving Congress's goals. Before Hatch-Waxman, only 19% of prescriptions were filled with generics. Now, that number is 90%. *See* FDA, *40th Anniversary of the Generic Drug Approval Pathway* (Sep. 23, 2024).[2] At the same time, innovative pharmaceutical companies have continued to drive the development of revolutionary new treatments, including discovering new uses for existing medications, such as treatments for chronic, complex, and rare diseases.

Yet Petitioners seemingly believe that Congress should have given them more than this fair balance. Petitioners argue that, as long as a "skinny" label avoids reciting the relevant claim language, the skinny label is non-inducing as a matter of law, and infringement allegations directed against that label must be dismissed at the pleading stage, regardless of what other statements the generic manufacturer makes about its product. The practical effect of Petitioners' standard would be that a skinny label could be deemed non-inducing as a matter of law regardless of any other allegations showing inducement in a particular case, and generic manufacturers would be granted license to make public statements about the patented use without risk of inducement liability.

Petitioners thus seek to upset the careful balance Congress created in Hatch-Waxman. They ask for a

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[2] https://www.fda.gov/drugs/cder-conversations/40th-anniversary-generic-drug-approval-pathway.

one-of-a-kind immunity from inducement liability, allowing generic manufacturers to promote the carved-out patented use in addition to the non-patented use approved by FDA, as long as certain magic words are not in their label. That is not the law. In Hatch-Waxman, Congress did not create special inducement rules for generic drugs. Instead, generic manufacturers are, and should be, subject to the same inducement liability as companies in all other industries. Congress certainly did not give generic manufacturers unreviewable discretion to decide for themselves whether their labeling statements constitute unlawful inducement. Nor did it allow them to make public statements concerning the patented use with impunity. Granting generic drug manufacturers these benefits would sharply depart from the careful framework Congress established in the Hatch-Waxman Act and make it more difficult for pharmaceutical companies to drive innovation.

A. Congress Struck a Careful Balance Between Permitting Generics to Enter the Market and Encouraging the Research and Development of Additional Indications.

To expedite generic drugs' path to market, Congress bestowed several advantages on generic manufacturers in the Hatch-Waxman Act. As relevant to this case, Congress created a statutory pathway allowing generics to come to market for non-protected uses while "carving out" protected uses from their labeling. *See* 21 U.S.C. § 355(j)(2)(A)(viii). It also allowed generics to obtain FDA approval based on the innovator manufacturer's approval, *see* 21 U.S.C.

§ 355(j), established a 180-day market exclusivity period for certain generic drugs, *see id.* § 355(j)(5)(B)(iv), and exempted generics from patent infringement liability for certain development work, *see* 35 U.S.C. § 271(e)(1).

Recognizing the risk that encouraging expansion of the generic drug market might stifle drug development innovation, Congress at the same time provided pharmaceutical companies with incentives for innovation. It granted innovator companies statutory exclusivities for eligible innovator drugs and permitted innovators to seek to restore some of the patent term lost due to the FDA approval process. *See* 21 U.S.C. § 355(j)(5)(F)(ii); 35 U.S.C. § 156. It generally required generic applicants to certify to innovator patents and provide notice of challenges to those patents, and it gave the innovator the opportunity to file an infringement suit to defend its patents against a challenge before a generic launch. 21 U.S.C. §§ 355(j)(2)(A)(vii), 355(j)(2)(B), 355(j)(5)(B)(ii).

And, critically, Congress maintained patent protections for method-of-use patents that remain in effect even if another indication for a drug is not patented. In designing its framework, Congress specifically contemplated situations in which a "listed drug may be approved for two indications." H.R. Rep. No. 98-857(I), at 22 (1984). In those situations, "[i]f the [generic] applicant is seeking approval only for indication No. 1, and not indication No. 2 because it is protected by a use patent, then the applicant must make the appropriate certification and a statement explaining that it is not seeking approval for indication No. 2." *Id.* Even the government concedes here

that this "availability of method-of-use patents provides an important incentive for continued research to identify additional therapeutic uses of established drugs." Br. for U.S. as Amicus Curiae Supp. Pet'rs 31 (filed Feb. 25, 2026) (U.S. Br.).

In other words, Congress allowed generic companies to obtain FDA approval of their drugs for *off-patent* uses and to market for only those uses. To obtain approval for so-called "skinny labeling" covering only unpatented uses of a drug, a generic manufacturer files a "Section viii" statement with the FDA as part of its abbreviated new drug application attesting that the indication for which the applicant is seeking approval is not a patented method of use. 21 U.S.C. § 355(j)(2)(A)(viii). The applicant must also submit its proposed labeling to the FDA omitting or carving out all methods of use claimed in a patent. 21 C.F.R. § 314.94(a)(8)(iv).

But Section viii is not about liability. Congress created a specific application requirement as an alternative to patent certification; it did not exempt filers from the Patent Act or any other law. Thus, the abbreviated FDA drug approval in no way diminishes patent protection over any patented method of use. As a result, generic manufacturers may be liable for patent infringement if they encourage use of their product for a patented use—whether in their labeling itself or in other statements, or both. *See* 35 U.S.C. § 271(b) ("Whoever actively induces infringement of a patent shall be liable as an infringer.").[3] And a suit

[3] This Court recently looked to Section 271(b) when analyzing contributory liability under copyright law. *See Cox Commc'ns,*

against a generic manufacturer may therefore proceed beyond a motion to dismiss so long as the complaint provides "enough facts to state" an inducement claim "that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007). Nothing in the Hatch-Waxman Act, the Patent Act, or general pleading standards suggests that the Section viii pathway constitutes a get-out-of-jail-free card for inducement liability. Indeed, the provision discussing Section viii statements simply requires generic applicants to include in their applications "a statement that the method of use patent does not claim" "a use for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(viii). It says nothing about this statement somehow relieving the applicant of inducement liability.

B. Petitioners Seek to Upset Congress's Balance, Grabbing More Benefits for Generic Drugs and Imperiling Valuable Multiple-Indication Innovation.

In keeping with the Hatch-Waxman Act's structure, Petitioners received FDA approval *only* for generic icosapent ethyl's unpatented use. That approval was conditioned on Petitioners marketing the generic drug only for the unpatented indication. Petitioners

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Inc. v. Sony Music Ent., 607 U.S. __, 2026 WL 815823, at *3 (2026). In that case, the plaintiff "provided no evidence of express promotion, marketing, and intent to promote infringement. And [the defendant] repeatedly discouraged copyright infringement by sending warnings, suspending services, and terminating accounts." *Id.* at *7. In contrast, here, Respondents pointed to specific statements and promotional activities in alleging induced infringement on the part of Petitioners.

now seek more than they are due under the Act—not just sales and promotion of their generic for the unpatented use, but immunity to promote the patented use, too.

It is important to emphasize what this case is *not* about. The Federal Circuit's decision did not cut back in any way on Petitioners' ability to sell their drug for the unpatented use. The Federal Circuit's decision merely recognizes that generic drug manufacturers may not use their labels, promotional materials, and public statements to promote a patented use. That Respondents are not attempting to stamp out use of the generic icosapent ethyl for non-patented uses is underscored by the fact that they have sued only one generic manufacturer for engaging in promotional activities that encourage use of icosapent ethyl for its patented use.

Nor is there any crisis in generic manufacturing requiring this Court's intervention. The Hatch-Waxman Act skyrocketed generic uptake in the United States—from 19% of prescriptions to 90%. *See 40th Anniversary of the Generic Drug Approval Pathway, supra.* Other metrics reinforce the prevalence of generics. For example, more than 80% of approved medications have generic versions available on the market, up from only 35% in the time before Hatch-Waxman. *See* PhRMA, *What is Hatch-Waxman?* (June 2018).[4] And generics often enter the market immediately upon patent expiration and are adopted rapidly—some capture as much as 90% of the market within three months. *Id.* Indeed, even when FDA

[4] https://perma.cc/4Y3G-LHBM.

approves a generic drug only for non-patented indications, it has long been the case that generic products are nevertheless used for patented indications through automatic substitution of generics for the listed drug, providing generic manufacturers with even more market penetration. *See* Jesse C. Vivian, *Generic Substitution Laws*, 33 U.S. Pharmacist 30 (2008) (describing automatic substitution for generic drugs).[5] Even though automatic substitution occurs, pharmaceutical companies are able to pursue innovation because of the protections for new uses.

In short, the Hatch-Waxman Act has succeeded in achieving Congress's goals: the United States has a robust generic drug market, and drug innovation continues. The Federal Circuit's decision in this case broke no new ground; the government's concern that "[u]ncertainty about [S]ection viii will deter generic manufacturers from invoking that mechanism" is therefore entirely misplaced. U.S. Br. 20.

There is thus no cause to contort either patent law or pleading standards to provide generic manufactures like Petitioners with *additional* market advantages beyond those fairly afforded by Congress. Indeed, although Petitioners contend their alleged statements do not amount to patent inducement, they fail to explain why they made the statements they did—preplanned and considered statements like press releases—if not to encourage use beyond the unpatented indication. Petitioners will have an opportunity at trial to convince a jury that they did not have

[5] https://perma.cc/D9BQ-6LUF.

the requisite intent to induce infringement; this case is solely about the adequacy of the pleadings.

C. Petitioners Propose Bright-line Immunity for Generic Drug Manufacturers to Encourage Infringing Use Through Their Promotional Materials and Statements to Investors.

In attempting to obtain more from the Hatch-Waxman Act than that scheme provides, Petitioners seek to turn Section viii into an immunity provision. They ask this Court to bless an approach that would in effect provide a safe harbor for generic manufacturers to promote their drugs for patented uses in public statements, so long as they do not expressly urge prescribers and patients to use the drug.

But that is not the statute that Congress enacted. The skinny-labeling provisions of Hatch-Waxman were never intended to provide generic manufacturers *carte blanche* to encourage using their drugs for patented indications. The congressional scheme for abbreviated FDA approval has always had as its counterbalance the legal prohibitions on patent infringement and inducement of such infringement, preserving for patentees their remedies under law to address infringement.

This Court should reject Petitioners' call for a bright-line rule that general statements cannot induce infringement and must be considered in isolation. Respondents allege that Petitioners intentionally induced infringement through their label *in combination with* statements in press releases

and on their website—including touting sales figures largely attributable to the patented indication and calling the product the "generic version" of a drug that is indicated "in part" for the unpatented indication. *See, e.g.*, JA42–43. Petitioners argue in contrast that—as a categorical rule—a case must be thrown out on a motion to dismiss if the generic manufacturer's communications do not each recite all the patent claim language or expressly encourage patients and prescribers to use the drug for the patented uses.

Ruling that a party is, as a matter of law, not liable for induced infringement unless it uses the claim language verbatim would fundamentally change inducement law across the board. Were Petitioners' pleading standard adopted, a generic manufacturer defendant could easily avoid liability for patent infringement by couching its references to patented uses in more general language, even though its intended audience would readily recognize what is being conveyed. Indeed, Petitioners here chose to rely on the language of a "generic version of Vascepa"—Respondents' trademark that uniquely identifies their product and indications—and chose to make references to the sales figures associated with Vascepa. If, however, patent infringement defendants know that courts will consider the full context of their public statements, they have less incentive to craft "wink-and-nod" messages designed to spur infringing uses while staying just shy of an explicit instruction.

The immunity Petitioners seek would also make generics the only actors in any patent-heavy industry that are insulated from inducement liability. Manufacturers of software, telecommunications equipment,

and the like remain bound by the standard rules governing the encouragement of infringing conduct. Those industries benefit from no safe harbors from infringement liability; in each, a court, looking at the totality of allegations, considers whether the plaintiff has stated an inducement claim. *See, e.g.*, *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1322 (Fed. Cir. 2009) (regarding software products, "[a] plaintiff may still prove the intent element [of induced infringement] through circumstantial evidence"); *Broadcom Corp. v. Qualcomm Inc.*, 543 F.3d 683, 700 (Fed. Cir. 2008) (regarding wireless voice and data communications patents, affirming a jury instruction to consider "all of the circumstances" relevant to the alleged induced infringement and concluding that "[t]aken as a whole," the record provided substantial evidence to support the jury verdict).

Indeed, under Petitioners' theory, innovator companies would lose their remedy for induced infringement of use patents, allowing generics to knowingly profit from infringing uses. Congress expressly authorized only one safe harbor in Hatch-Waxman: the safe harbor from infringement codified in 35 U.S.C. § 271(e)(1), which states that "[i]t shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." This provision overruled *Roche Product, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858 (Fed. Cir. 1984)), and created a safe harbor for such development and submission activities. *See* H.R.

Rep. No. 98-857(I) (1984). Section 271(e)(1) demonstrates that when Congress meant to enact a safe harbor in this context, it expressly did so. Yet Congress did not enact a safe harbor in the context of inducement liability for skinny labels. Generic manufacturers' attempt to add a *second* safe harbor not contemplated by Congress as part of the Hatch-Waxman compromise should be rejected.

Maintaining the balance struck by Congress is particularly important in the biopharmaceutical industry, where the incentives to develop new, clinically meaningful uses are fragile and the stakes for patients are profound. As explained in more detail, *infra* Section II, the research necessary to bring a second indication to market is long, expensive, and uncertain. Companies cannot justify investing millions of dollars and years of effort only to be governed by a regime where a generic competitor can promote the patented use with impunity.

D. Embracing Petitioners' Position Would Leave Generic Manufacturers to Effectively Be the Final Judges of Their Own Carveouts.

A decision from this Court holding that a pharmaceutical company plaintiff does not even state a claim for induced patent infringement when it details multiple statements by the defendant referring to the infringing use gives generic manufactures an extra-statutory safe harbor, as explained *supra* Section I.C. It also prevents judicial factfinders from determining whether labels and promotional statements, considered together or taken separately, constitute unlawful

inducement. Without the policing of courts, generic manufacturers would be free to decide—without oversight—that their labeling and marketing does not unlawfully encroach on patented uses.

The briefs of other parties are replete with statements asserting—or assuming—that Petitioners drafted a properly skinny label. *See, e.g.*, U.S. Br. 11 ("FDA approved Hikma's ANDA, including its carved-out or 'skinny'" labeling"); *id* at 26 ("Hikma's skinny labeling cannot properly be treated as evidence of culpable encouragement to infringe."). These briefs elide the fact that Respondents' inducement allegations relied in significant part on Petitioners' statements extrinsic to the label (as evidenced by the fact that Respondents have not sued other generics who carved out the patented indication). But the adequacy of Petitioners' carveout is also a disputed factual question in the case. Respondents asserted that Petitioners' label encouraged use of the generic drug for the patented use. *See* Compl. ¶¶ 130–135, *Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 2021 WL 9316574 (D. Del. filed Jan. 25, 2021). If generic manufacturers could self-certify that their labeling is properly "skinny" without fear of inducement liability, they would have unchecked discretion to discuss patented uses in their labeling.

FDA's review of the proposed skinny label is no stand-in for judicial review. FDA does not police inducement; courts do. Rather, FDA's role is a regulatory one—it determines whether the drug is the same and bioequivalent to the listed drug for the requested indication and whether the label accurately reflects the non-patented approved use. FDA takes a Section

viii statement at face value. It does *not* evaluate whether a proposed generic label infringes any patent, and FDA approval does *not* confirm that the label, or the marketing materials for the label, complies with patent law. *See GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320, 1332 (Fed. Cir. 2021) ("FDA plays no role in determining patent infringement"). When Petitioners suggest that FDA's acceptance of the Section viii carve-out somehow validates their position, they therefore misrepresent the statutory scheme and FDA's role within it.

Consistent with that statutory scheme, FDA has made clear that its role in the approval process does not remove the need for generic manufacturers to evaluate their potential for liability under the patent laws. As FDA has explained, the FDA "use code," a standardized descriptor that links a specific patent to an FDA-approved method of using a drug, "is not intended to substitute for the . . . ANDA applicant's review of the patent and the approved labeling." Abbreviated New Drug Applications and 505(b)(2) Applications, 81 Fed. Reg. 69,580, 69,598 (Oct. 6, 2016); *see also Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 403 (2012) ("[T]he FDA requires brand manufacturers to submit descriptions of the scope of their patents, known as use codes. The FDA does not attempt to determine if that information is accurate."); *see* U.S. Br. 7 (describing use codes in FDA approval process). Any suggestion otherwise misconstrues the administrative function of the tools at FDA's disposal.

FDA's role is limited, as it acknowledges. FDA lacks the expertise, resources, and statutory

authority to review labeling or marketing materials for generic products to ensure they avoid patent infringement by construing patent claims and adjudicating infringement issues. Indeed, FDA itself observed that "[a] fundamental assumption of the Hatch-Waxman Amendments is that the courts are the appropriate mechanism for the resolution of disputes about the scope and validity of patents." Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,683 (June 18, 2003).

These legal questions are left with the courts because courts possess the expertise necessary to evaluate pharmaceutical patent infringement suits, just as they do with respect to all other industries. Claim construction usually requires fact development and expert testimony. Whether a generic drug manufacturer induced infringement through its label and promotional activities is a matter of patent enforcement. That oversight is firmly within the purview of the federal judiciary. And this is especially important in the Section viii context, which affords the patent holder no other opportunity to weigh in on the proposed skinny label; indeed, the patent holder does not even receive advance notice of a generic's skinny label. *Compare* 21 U.S.C. § 355(j)(2)(B) (requiring notice to the patent holder under a different mechanism under the Hatch-Waxman Act) *with* 21 U.S.C. § 355(j)(2)(A)(viii) (containing no notice requirement for a Section viii statement).

As a final matter, *amici curiae* urge this Court—whatever resolution it reaches in this particular case—not to create a self-policed safe harbor for a self-declared skinny label and its marketing materials.

Even if the outcome in this case is favorable to Petitioners, the inquiry in future cases should remain fact-specific and governed by an evaluation of the totality of the allegations in a particular complaint.

II. Immunizing Petitioners' Infringing Statements, Including in Claimed Skinny Labeling, Would Disrupt Investment and Discourage the Discovery of New Uses for Existing Drugs.

As explained, the Federal Circuit's decision should be upheld because it properly engaged with the allegations in the complaint just as it would in any other patent inducement suit and its ruling poses no threat to the benefits provided to generic manufacturers under the Hatch-Waxman Act as properly understood. Overturning that decision, in contrast, would impede American drug innovation and threaten potentially devastating consequences. Companies make investment decisions in reliance on enforceable use patents, and the investments are made with the understanding that the courts—not the generic competitors—will determine whether inducement has occurred.

The biopharmaceutical industry, and the patients it serves, depend on sustained investment in and continued pursuit of new drug therapies, in reliance on enforceable use patents. This pursuit includes, but is not limited to, new therapeutic uses for medicines already approved for a particular indication. Unlocking additional indications has achieved significant medical breakthroughs in treating, for example, cancer and rare diseases. At times, these transformative

treatment benefits have far exceeded the first approved use in terms of economic value to the innovator and therapeutic value to the patients. And that work is far from over. Using screening technologies, researchers have identified hundreds of drugs that have the potential for additional indications. *See* Benjamin N. Roin, *Solving the Problem of New Uses*, at 42 (Oct. 1, 2013).[6]

But innovation does not come easily or cheaply. It demands substantial post-approval investments in scientific research and drug development—amounting to hundreds of millions of dollars and years of study—undertaken amid significant uncertainty. Regardless of whether a new-indication patent issues, automatic substitution will result in dispensing of generic versions to patients for all indications, including the patented one, the moment a generic enters the market. Under current law, those effects are partially offset by the ability to pursue induced infringement claims when a generic manufacturer actively promotes or knowingly facilitates infringing use through its statements, labels, and marketing.

Permitting generic manufacturers to infringe pharmaceutical patents on indications by encouraging use of generic drugs for patented uses would further diminish incentives for innovation. Pharmaceutical companies strive to provide the best medicines for American patients, but they are also economic actors who must consider returns on investments as well as their duties to shareholders. Without meaningful patent protection for additional

[6] https://dx.doi.org/10.2139/ssrn.2337821.

indications for existing medicines, potential returns are unlawfully limited and innovation will suffer, harming patients in the process. Indeed, if pharmaceutical companies are deprived of any real mechanism to seek court review of whether a generic manufacturer is inducing infringement of a patented use, those companies will be forced to reevaluate their investment decisions with respect to existing medications—and potentially even with respect to pre-approval innovation as well. They may choose not to take on the risk and invest the time and money necessary to achieve the next breakthrough indication.

A. Incentivizing Innovation Beyond First-Approved Indications Promotes Public Health.

Innovative pharmaceutical companies often continue to study their products for additional indications after FDA approval. Discoveries emerging from that research and investigation have reshaped standards of care, addressed serious unmet medical needs, and delivered meaningful benefits to millions of patients.

1. Post-Approval Research and Development Is a Vital Source of New, Improved Treatment Options.

Innovation after a first approval plays an indispensable role in advancing patient treatment. More than half of small molecule medicines approved between 2006 and 2012 received FDA approval for at least one additional post-approval new use. *See* P'ship for Health Analytic Rsch., *Implications of the*

Inflation Reduction Act Price Setting Provisions on Post-approval Indications for Small Molecule Medicines 2 (June 2023).[7] Among cardiovascular medicines, for example, approximately half of all approved uses and three-quarters of industry-funded clinical trials occurred post-approval. *See* Henry Grabowski & Genia Long, *Post-Approval Indications and Clinical Trials for Cardiovascular Drugs: Some Implications of the US Inflation Reduction Act*, 27 J. Med. Econ. 463, 466 (2024).[8] And "small-molecule drugs used to treat conditions related to oncology, cardiology, and immunology" were prescribed to patients about twice as often as they were prescribed for the initial indication. Empl. Benefit Rsch. Inst., *What Employers Should Know About the Inflation Reduction Act and Drug Development* 2 (May 1, 2025).[9] About 35% of prescriptions were associated with the initial approval, while 65% were associated with one of the medicine's subsequent indications. *Id.*

The evolution of new cancer therapies underscores just how essential post-approval research is to advancing patient care. Post-approval research and development is *the main source* of new cancer treatments—the majority of cancer research and development occurs after initial approval. For oncology drugs approved from 2000 to 2021, more than half of all indications approved and approximately two-thirds of industry-funded clinical trials occurred after the first approval of the drug. Henry Grabowski, Joseph A.

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[7] https://perma.cc/UCY8-9A4U.

[8] https://doi.org/10.1080/13696998.2024.2323903.

[9] https://perma.cc/Q7XT-3USF.

DiMasi & Genia Long, *Postapproval Innovation for Oncology Drugs and the Inflation Reduction Act*, 43 Health Affs. 1400, 1400 (2024).[10]

The importance of post-approval research and development is in part due to the nature of cancer, the manner in which research on the value and benefits of a medicine is conducted, and the way that scientific evidence accumulates over time. *See* PhRMA, *Emerging Value Report* (July 2023).[11]

First, post-approval research and development often reveal shared features in different cancers, which informs potential new uses of existing medicines. *See* Daniel Tobias Michaeli et al., *Initial and Supplementary Indication Approval of New Targeted Cancer Drugs by the FDA, EMA, Health Canada, and TGA*, 40 Investigational New Drugs 798, 798 (2022) (*Initial and supplementary indication approval*).[12] For example, in 2011, FDA granted accelerated approval to crizotinib to treat patients with locally advanced or metastatic non-small cell lung cancer whose tumors had an abnormality leading to cancer cell growth caused by changes in a particular gene. *See* Pfizer, *U.S. Food and Drug Administration Approves Pfizer's XALKORI® (crizotinib) As First and Only Therapy Specifically for Patients with Locally Advanced or Metastatic ALK-Positive Non-Small Cell Lung Cancer* (Aug. 26, 2011).[13] Similar changes in that gene then

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[10] https://doi.org/10.1377/hlthaff.2024.00202.

[11] https://perma.cc/ARN3-6YTC.

[12] https://doi.org/10.1007/s10637-022-01227-5.

[13] https://perma.cc/YP62-TSKM.

were discovered in tumors across cancer types, prompting researchers to study crizotinib's untapped potential. *See* Pfizer, *Pfizer's XALKORI® (crizotinib) Approved by FDA for ALK positive Anaplastic Large Cell Lymphoma in Children and Young Adults*, (Jan. 14, 2021) (*XALKORI Approved*);[14] *see* FDA, *FDA approves crizotininib for ALK-positive inflammatory myofibroblastic tumor* (July 14, 2022).[15] That research paid off. FDA has since greenlit multiple additional indications—some coming a full decade after initial approval—expanding treatment to adults and pediatric patients with rare cancer types. *See XALKORI Approved, supra.*

Second, researchers typically begin cancer research and development in narrowly defined patient populations with advanced stages of cancer—those who have exhausted all other treatment options. But if that medicine proves to be safe and effective, researchers may seek to introduce the medicine to patients at earlier stages, where a new treatment is more likely to significantly modify the course of the disease and may even halt its progression. *See generally* IQVIA Inst., *Global Oncology Trends 2022* (May 26, 2022);[16] *Initial and Supplementary Indication Approval, supra*; David Crosby et al., *Early Detection of Cancer*, 375 Sci. 1244, 1244 (2022).[17] Abemaciclib, for

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[14] https://perma.cc/Z2L4-8NYL.

[15] https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-crizotinib-alk-positive-inflammatory-myofibroblastic-tumor.

[16] https://doi.org/10.13140/RG.2.2.11901.06882.

[17] https://doi.org/10.1126/science.aay9040.

example, was originally approved to treat advanced or metastatic breast cancer that had progressed following hormone therapy. *See* FDA, *FDA approves new treatment for certain advanced or metastatic breast cancers* (Sept. 28, 2017) (republished in PR Newswire).[18] After additional clinical research, it was later approved to treat the most common subtype of early breast cancer: HR+ HER2-. That approval marked the first new treatment of its kind in nearly two decades, and the first and only medicine in its class approved for patients with that subtype. *See* Lilly Investors, *FDA Approves Verzenio® (abemaciclib) as the First and Only CDK4/6 Inhibitor for Certain People with HR+ HER2- High Risk Early Breast Cancer* (Oct. 13, 2021).[19] Recent data confirm that abemaciclib significantly improves overall survival in patients with this type of early breast cancer, making it the first CDK4/6 inhibitor to demonstrate that reducing the risk of recurrence translates into improved overall survival, and "mark[ing] [a] major milestone in the development of effective therapies that have the potential to cure more patients with this common form of breast cancer." Stephen Johnston et al., *Overall Survival with Abemaciclib in Early Breast Cancer*, 37 Annals Oncol. 156, 162 (2026).[20]

Third, post-approval research and development can lead to a greater understanding of the safety and efficacy of combining multiple medicines as compared to a single therapy. *See* Deborah Plana, Adam C.

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[18] https://perma.cc/H77M-9UUW.

[19] https://perma.cc/W23L-ZZCJ.

[20] https://doi.org/10.1016/j.annonc.2025.10.005.

Palmer & Peter K. Sorger, *Independent Drug Action in Combination Therapy: Implications for Precision Oncology*, 12 Cancer Discov. 606, 606–07 (2022).[21] That benefit is particularly important for treating cancers, where patients often need a combination of treatments to attack the disease on multiple fronts and prevent treatment resistance. A single drug might not be effective in eradicating every cancer cell in a tumor—it might target some, or even a majority, of a certain type of cells but leave behind resistant cells, which then repopulate the tumor. *See id.* at 607. Drug combinations, in contrast, can target different subsets of cells, which improves both the efficacy and the durability of the treatment. *See id.* The same goes for treatments across different patients: a single therapy will not be effective in every patient, but combination therapies provide patients with opportunities for a clinically meaningful response. *See id*. Post-approval research is necessary to determine the availability of these combination treatments.

Finally, post-approval research and development help shed light on the full therapeutic value of a particular cancer treatment. Overall survival is considered the "gold standard" for evidence of a cancer drug's safety and effectiveness, but it can take years of follow up with patients to determine if a treatment actually prolongs patients' lives. Margret Merino et al., *Irreconcilable Differences: The Divorce Between Response Rates, Progression-Free Survival, and Overall Survival*, 41 J. Clin. Oncol. 2706, 2706 (2023).[22] As

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[21] https://doi.org/10.1158/2159-8290.CD-21-0212.

[22] https://doi.org/10.1200/JCO.23.00225.

a result, beneficial evidence of a treatment's safety and effectiveness can emerge years after a drug first reaches the market, through continued investment in post-approval research.

The long-term clinical development needed to discover these additional uses involves years of research, significant risk, and substantial financial investment. Without post-approval research and development—and the necessary incentives to enable it—these medications would never have expanded beyond their original uses.

2. Novel Indications May Prove Even More Consequential Than the First.

Post-approval research and development do not just drive development within the same therapeutic area; they have also resulted in transformative new uses and treatments in different diseases, including on a scale the original indication never approached. New uses of approved medicines have provided critical treatment advances, particularly for cancer patients, children, and those impacted by rare diseases. Many of these post-approval research advances brought first-time treatments for patients.

Take Respondents' product, Vascepa. Respondents seek to enforce their patent on a subsequent patented use approved by the FDA. Vascepa began as a triglyceride-lowering therapy in patients with very high triglycerides and has evolved into a major cardiovascular-risk-reduction drug. After obtaining approval on an initial indication that covered a limited

patient population,[23] Amarin invested in a "[l]andmark" trial that included over 8000 patients and lasted nearly five years, *see* Amarin, *Vascepa: Benefits, Clinical Trial Results* (2024).[24] That trial revealed "groundbreaking" results showing that, when used together with cholesterol medications known as statins, Vascepa reduced cardiovascular events by *roughly 25%*. *Id.* Those results far exceeded the clinical impact of the initial hypertriglyceridemia indication. And there had previously been no proven way to reduce persistent cardiovascular risk for this population of cardiovascular patients with high triglycerides. *Id.* Vascepa became the first and only medication approved by FDA for that purpose. *Id.*

Similar examples exist across therapeutic areas. In 2022, FDA approved a new indication for an existing medicine that became the first approved therapy targeted to "HER2-low" breast cancer—a form of breast cancer that historically has had limited treatment options. *See* FDA, *New Drug Therapy Approvals*

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[23] *See Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 449 F. Supp. 3d 967, 983 (D. Nev.) (noting first indication trial included only 151 patients), *aff'd*, 819 F. App'x 932 (Fed. Cir. 2020); *see also Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 104 F.4th 1370, 1374 (Fed. Cir. 2024) ("[T]he CV indication ... undisputedly made up more than 75% of the drug's sales."); Compl. ¶ 152, *Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 2021 WL 9316574 ("Available market data indicates that less than 10% of the prescriptions of VASCEPA® are currently in the Severe Hypertriglyceridemia population and thus could be covered under the Severe Hypertriglyceridemia Indication.").

[24] https://perma.cc/AQ8L-ZRTR.

(Jan. 2023).[25] The same year, two treatments were newly approved for use in combination to treat pediatric patients whose tumors express a BRAF mutation. *See id.* The list goes on. *See id.* (collecting notable approvals for new uses or indications of approved drugs).

And this is not a new phenomenon. In 1986, interferon was approved for hairy cell leukemia, a very rare cancer. *See* Lawrence M. Fisher, *Interferon Set to Treat Hepatitis*, N.Y. Times (Feb. 26, 1991). Five years later, interferon was approved to treat hepatitis C—a contagious disease for which there was no reliable therapy. *See id.* Interferon became the standard of care in hepatitis C treatment for years.

3. Post-Approval Research Has Led to New Treatments for Rare Diseases with Unmet Medical Need.

Discovering treatments for rare diseases is a top public health priority. Rare diseases can be life-threatening, and most do not have approved treatments. An estimated 10,000 rare diseases affect approximately one out of every ten Americans—more than 30 million people. Half of those affected are children. *See* FDA, *Rare Disease Innovation Hub* (Feb. 2, 2026).[26]

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[25] https://www.fda.gov/drugs/novel-drug-approvals-fda/new-drug-therapy-approvals-2022.

[26] https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fda-rare-disease-innovation-

Post-approval research and development are essential for advancing new treatments for rare diseases. Nearly 30% of all post-approval uses treat patients with rare diseases. *See* IQVIA Inst., *Proliferation of Innovation Over Time*, at 14 (Feb. 18, 2025).[27] And 35% of drugs for rare diseases—known as "orphan-designated" drugs—have a post-approval indication in a new disease. *See* Kathleen L. Miller & Michael Lanthier, *Orphan Drug Label Expansions: Analysis of Subsequent Rare and Common Indication Approvals*, 43 Health Affs. 18, 20 (2024).[28]

To take some examples, the first approved treatment for symptoms of Bardet-Biedl syndrome, a rare genetic disorder, emerged from an existing medicine. *See New Drug Therapy Approvals, supra.* As did the first approved treatment for pediatric patients with juvenile myelomonocytic leukemia, a rare and aggressive blood cancer primarily affecting young children. *See id.* And in 1985, leuprolide acetate was approved as a palliative treatment for advanced prostate cancer; less than ten years later, it was approved to treat central precocious puberty, a rare disease in children under the age of nine. Rajni Sethi & Nicholas Sanfilippo, *Six-Month Depot Formulation of Leuprorelin Acetate in the Treatment of Prostate Cancer*, 4 Clinical Interventions Aging 259, 261 (2009).[29] Without the sponsor's investment in a second medical use,

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hub#:~:text=An%20estimated%2010%2C000+%20rare%20diseases,and%20Office%20of%20Combination%20Products./.

[27] https://perma.cc/BV7X-R3WU.

[28] https://doi.org/10.1377/hlthaff.2023.00219.

[29] https://doi.org/10.2147/cia.s4885.

treatment options for these rare diseases would not exist, and patients would be deprived of potentially life-saving medicines.

4. Investing in Additional Uses Can Have Significant Benefits.

Clinical trials for second indications provide authoritative evidence of safety and efficacy beyond the research necessary to obtain an initial approval. This in-depth clinical research creates confidence in a particular medication and ensures that it is safe and effective for patients for the new use. The alternative is that the manufacturer never invests in a second indication, but doctors nevertheless prescribe the medication "off-label" without any (or insufficient) safety and efficacy studies on that particular use.

Some of the most important insights into a drug's potential occur after approval; indeed, some questions can be answered only after a drug is approved. *See* Ali Abbasi, Donna Rivera, Lesley H. Curtis & Robert M. Califf, *Post-Approval Evidence Generation: A Shared Responsibility for Healthcare*, 30 Nature Med. 3046, 3047 (2024).[30] Questions of comparative effectiveness, for example, are rarely resolved at the time of approval because the standard of care is constantly evolving and context specific; a comparator used in pre-approval trials is not necessarily the alternative option actively considered by doctors and patients after a drug reaches the market. *Id.* And continued research often sheds greater light on a drug's safety,

[30] https://doi.org/10.1038/s41591-024-03241-x.

especially given the length of time required for the completion of some clinical trials. *Id.*

All of this reflects a simple but important reality: protecting the exclusivity afforded by a grant of a patent—and therefore return on investment—of subsequent indications strengthens patient safety and public health. It promotes the rigorous research and clinical studies needed to understand a therapy's full clinical value and supports the evidence-backed treatments patients turn to most frequently.

B. Drug Innovation Requires Massive Investments in Post-Approval Research That Will Be Inhibited If Generic Manufacturers Are Permitted to Infringe Patented Uses.

Securing a second indication is not simply an extension of the first; it often represents a new—and sometimes even bigger—financial bet. Post-approval development regularly requires massive investments, multi-year clinical programs, and large outcome trials designed to generate the evidence needed to affirm a medicine's safety and efficacy for a new purpose.

Novel indications can require large, expensive outcome trials—especially for common conditions. These trials deliver outsized population-health gains, across safety, efficacy, and appropriate use. Most approvals of additional indications are supported by Phase III trials. Based on trial data from both new and existing molecules, some estimates put the cash outlay for a Phase III clinical trial at $31.3 to $214.4 million across therapeutic areas. *See* Aylin Sertkaya,

Trinidad Beleche, Amber Jessup & Benjamin D. Sommers, *Costs of Drug Development and Research and Development Intensity in the US, 2000-2018*, 7 JAMA Network Open 1, 7 (2024) (using 2018 dollars).[31] This cost represents solely the expense of running a trial, not incorporating the costs of failures. Other estimates set the mean total cash outlay for Phase III at $255.4 million based on data from new molecules. *See* Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. Health Econ. 20, 24 (2016).[32]

As explained above, pharmaceutical companies are able to make these substantial investments, even in the face of meaningful scientific uncertainty, in reliance on their ability to protect against induced infringement. Companies understand that on the other end of hundreds of millions of dollars and a decade or more of research, the novel use that they discover can be protected, even as generics enter the market.

Although in reality generic drugs are often dispensed as substitutes for the prescribed innovator drug, under existing law generic manufacturers are not immunized from infringement liability, and patent owners can address infringement through all the tools provided in the Patent Act. Under Petitioners' proposed rule, however, any generic that files a Section viii statement and has an allegedly skinny label would be categorically immunized from inducement

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[31] https://doi.org/10.1001/jamanetworkopen.2024.15445.

[32] https://doi.org/10.1016/j.jhealeco.2016.01.012.

liability, no matter how it encourages infringement through its statements or marketing. Petitioners thus seek to turn Section viii into an express immunity ticket, effectively taking away remedies Congress chose to make available to patent owners. Doing so would amplify the effects of automatic substitution and erode innovation incentives beyond the status quo.

Pharmaceutical companies cannot rationally invest in developing new uses if, on the other side, they will be denied the opportunity to obtain meaningful judicial review of whether a generic manufacturer induced infringement. Petitioners' position thus undermines the legal protections that are necessary for pharmaceutical companies to justify continued investment in developing lifesaving new treatments.

* * *

Congress has already struck the balance between expediting generic drugs' market entry and assuring patent protections for later-approved indications. The Federal Circuit's decision respected that balance, applying generally applicable patent and pleading principles to the case before it. Petitioners instead invite this Court to create a bright-line safe harbor for infringing statements that has no statutory basis. The Court should decline the invitation; regardless of how it rules on the facts of this case, the Court should make clear that generic manufacturers are subject to the same rules governing infringement inducement as manufacturers in other industries.

CONCLUSION

The Federal Circuit's decision should be affirmed.

Respectfully submitted,

David E. Korn
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA
670 Maine Ave., SW
Washington, DC 20024
(202) 835-3400

Sarah E. Harrington
Counsel of Record
Michael N. Kennedy
Krista H. Carver
COVINGTON & BURLING LLP
850 Tenth Street, NW
Washington, DC 20001
(202) 662-6000
sharrington@cov.com

Joseph B. Franklin
John T. Delacourt
BIOTECHNOLOGY INNOVATION ORGANIZATION
1201 New York Ave., NW
Washington, DC 20005

Charlotte S. Butash
COVINGTON & BURLING LLP
30 Hudson Yards
New York, NY 10001

March 27, 2026