No. 22-37

In The
Supreme Court of the United States

TEVA PHARMACEUTICALS USA, INC.,
Petitioner,

v.

GLAXOSMITHKLINE LLC,
SMITHKLINE BEECHAM (CORK) LIMITED,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

BRIEF OF *AMICUS CURIAE* ALVOTECH IN SUPPORT OF PETITIONER

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QUESTION PRESENTED

If a generic drug's FDA-approved label carves out all of the language that the brand manufacturer has identified as covering its patented uses, can the generic manufacturer be held liable on a theory that its label still intentionally encourages infringement of those carved-out uses?

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INTEREST OF *AMICUS CURIAE*[1]

Alvotech USA Inc. and Alvotech hf. (collectively, Alvotech) focus on developing and manufacturing high-quality biosimilar medicines, *i.e.*, biopharmaceutical medicines that have been shown to be "highly similar" to, and have no clinically meaningful differences from, a reference biologic medicine. Alvotech aims to improve access to biosimilars, believing that if there is a proven biologic medicine, it should be accessible to all patients in need. Alvotech has made substantial investments developing unique cell lines, unique manufacturing processes, and unique formulations as compared with reference biologic medications with the goal of bringing affordable biosimilar treatments to patients in the U.S. and beyond.

Alvotech has a significant interest in the question presented in Teva Pharmaceuticals USA, Inc.'s petition for a writ of certiorari. In the decision below, the Federal Circuit upheld a massive jury verdict against petitioner for inducing infringement of a patent covering a patented indication by marketing and selling a generic drug approved only for *un*patented indications. By cobbling together disparate statements from the generic label's description of its unpatented indications and truthful statements from product materials about the generic's FDA approval, the court affirmed

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[1] Pursuant to Rule 37.6, *amicus curiae* affirms that no counsel for a party authored this brief in whole or in part and that no person other than *amicus curiae* or its counsel made a monetary contribution to its preparation or submission. Counsel of record for all parties were timely notified pursuant to Rule 37.2(a) of *amicus curiae*'s intent to file this brief, and all parties have provided written consent to its filing.

a jury verdict equal to more than three times *all* of petitioner's $74 million in sales of the generic for *all uses* during the relevant period. As a result, the Federal Circuit's decision provides ammunition for brand-name biologic companies to threaten and pursue similar litigation against biosimilar companies, impeding and delaying the launch of new biosimilars and imposing unnecessary costs on consumers, the government, and biosimilar companies.

INTRODUCTION AND SUMMARY OF ARGUMENT

1. America is in the midst of a drug-pricing crisis. A 2019 Gallup study found that more than 13% of American adults (over 34 million people) know at least one friend or family member who died in the past five years because they could not afford medical treatment. The same study found that 58 million Americans had experienced "medication insecurity" (the inability to pay for prescribed medication) at least once in the past twelve months. *See* Dan Witters, *Millions in U.S. Lost Someone Who Couldn't Afford Treatment*, GALLUP (Nov. 12, 2019), https://bit.ly/3SAYtQn. Nationwide spending on medication has increased from $195 billion just 20 years ago to over $574 billion in 2021. *See* IQVIA Institute, *Total nominal spending on medicines in the U.S. from 2002 to 2021*, STATISTA (Apr. 2022), https://bit.ly/3zAOCla.

Brand-name drugs are the primary driver of these rising prices. *See* IQVIA Institute, *Proportion of branded versus generic prescription drug spending in the United States from 2017 to 2021*, STATISTA (Apr. 2022), https://bit.ly/3P0JjRr. According to the 2021 Congressional Committee on Oversight and Reform

Drug Pricing Investigation, in the five-year period from 2016 and 2020, pharmaceutical companies raised the price of branded prescription drugs by 36%—almost four times the rate of inflation during that period. STAFF OF H. COMM. ON OVERSIGHT & REFORM, 117th Cong., Drug Pricing Investigation at iii (Maj. Staff Rep. Dec. 2021), https://bit.ly/3Q7Yolx (*Drug Pricing Investigation Report*). These price hikes correspond with a dramatic increase in patenting activity and aggressive use of the patent system by the pharmaceutical sector. *See id.* at 79-80, 107.

The Federal Circuit's decision in this case provides branded companies a new opportunity to take advantage of the patent system to the detriment of the nation's healthcare system and the American people. By upholding a massive infringement verdict based on a cobbled together collection of disparate references in a skinny label and truthful product materials, the decision below provides incentives for branded companies to use litigation and threats of litigation in an attempt to delay the launch of *un*patented drugs with *un*patented indications that compete with the brand product and provide important consumer benefits. The decision below concerned the chemical pharmaceutical market. But the threat of such behavior from branded companies will exist at least as much in the biopharmaceutical market.

2. Indeed, the consequences of the decision are likely only to be worse for biopharmaceuticals. Biopharmaceuticals—both brand-name biologics and biosimilars—are large-molecule pharmaceutical products "derived from natural, biological sources such as animals or microorganisms." *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1669 (2017). Brand-name biolo-

gics are among the most expensive medicines in the United States—representing only two percent of all prescriptions but more than half of all pharmaceutical spending. Biosimilars are "generic" versions of biologics, governed by a legal framework similar to the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act), including a similar abbreviated approval process for new drugs that are highly similar to an already-approved branded drug.

Because brand-name biologics are among the most expensive and top-selling medicines in the United States, lower-cost biosimilars are able to drive significant savings by entering the market and ending the monopoly power of the branded product. By providing lower-cost drugs and competition, biosimilars have provided an estimated $12.6 billion in savings since the first U.S. biosimilar was approved 10 years ago. Association for Accessible Medicines, *The U.S. Generic & Biosimilar Medicines Savings Report*, October 2021, at 17, https://bit.ly/3d1nkMY (*AAM Savings Report*). They have also been used in more than 121 million days of patient therapy and have supported almost 10 million incremental days of therapy—care that many patients would not have received without the availability of lower-cost biosimilars. *Id.*

Several differences between the markets for small-molecule drugs and biologics and between their respective legal regimes are likely to amplify the harm of the decision below for the biopharmaceuticals market. First, because the prices of biologics are several times higher than those of traditional chemical drugs, the threat of new litigation under the decision carries with it an increased threat of lost-profit damages. Second, the Federal Circuit's decision exacerbates the

harm from pre-existing patent strategies in biopharmaceuticals that tend to increase the number of patents covering a given biologic, which may now be asserted in new aggressive litigation by the biologic. And third, because biologics are not required, in seeking FDA approval, to identify publicly the patents that cover their on-label indications, biosimilars will likely find it even more difficult than generics to craft their labeling in a manner that might guard against the threat of litigation created by the decision below.

The net result is likely to undermine the pro-competitive design of the BPCIA and lead to decreased competition in the biopharmaceuticals market, increased prices of already prohibitively expensive pharmaceuticals, and, ultimately, reduced patient access to life-saving medications—to the detriment of the public health and welfare of the United States. The Court's intervention is warranted now.

ARGUMENT

If left intact, the Federal Circuit's decision can only worsen America's drug-pricing crisis. The decision below provides branded drug companies unwarranted new ammunition in their attempts to prevent or delay the launch of *un*patented drugs for *un*patented on-label indications that would compete with their own drugs. The ultimate victims of those efforts are the consumers who would otherwise enjoy greater access to life-saving and life-enhancing medicines at lower cost. And the harmful effects of the decision are likely only to be worse in the biopharmaceutical market, in light of both natural and legal differences between that market and the market for traditional, chemical pharmaceuticals. Further review is warranted.

I. Biosimilars Provide Vital Consumer Benefits Comparable to Generic Pharmaceuticals Under a Similar Legal Framework.

A. Biosimilars drive substantial savings and health benefits by competing with branded biologics.

Biopharmaceuticals, commonly known as biologics, are pharmaceutical products manufactured in living organisms. *See* Kasey E. Koballa, *The Biologics Price Competition and Innovation Act: Is a Generic Market for Biologics Attainable?,* 9 Wm. & Mary Bus. L. Rev. 479, 482 (2018). Unlike small-molecule drugs made through chemical, synthetic processes, biologics are large-molecule drugs made through less predictable manufacturing techniques in natural sources like plants, animals, and microorganisms. *See id.* Like their chemical counterparts, biologics offer important treatments for chronic conditions, including cancers, autoimmune diseases, and other serious health conditions. Examples of biologics and some of their approved indications include adalimumab (brand name Humira®) for rheumatoid arthritis or plaque psoriasis, trastuzumab (brand name Herceptin®) to treat early-stage HER2-positive breast cancer, and insulin glargine (brand name Lantus®) for type 2 diabetes. *See* Cong. Research Serv., *Biologics and Biosimilars: Background and Key Issues*, 26 (2019), https://bit.ly/3dnMXrF.

Brand-name biologics are among the most expensive medicines in the United States—representing only two percent of all prescriptions but more than half of all pharmaceutical spending. *See AAM Savings Report* 19. And these costs have only risen in recent

years. The average cost of a biologic has been as much as $45 per day, compared with $2 per day for other pharmaceuticals, with biologics costing anywhere from $10,000 to almost $250,000 annually per patient. *See* Erwin Blackstone and P. Fuhr Joseph, *The Economics of Biosimilars*, 6 AM. HEALTH DRUG BENEFITS 469 (2013); *Drug Pricing Investigation Report* vi.

Biosimilars are the lower cost, "generic" versions of costly brand-name biologics. Because brand-name biologics are among the most expensive and top-selling medicines in the United States, lower-cost biosimilars are able to drive significant savings by entering the market and ending the monopoly power of the reference product. By providing lower-cost drugs and competition, biosimilars drove an estimated $7.9 billion in savings to U.S. consumers in 2020 alone, and have provided an estimated $12.6 billion in savings since the first U.S. biosimilar was approved 10 years ago. *AAM Savings Report* 17. And those savings are just beginning: savings from biosimilars are projected to reach $133 billion in the next 5 years. *Id*. at 12.

Beyond providing significant savings for patients and payers, biosimilars also dramatically increase patient access to care. Since their introduction, biosimilars have been used in more than 121 million days of patient therapy and have supported almost 10 million incremental days of therapy—care that many patients would not have received without the availability of lower-cost biosimilars. *AAM Savings Report* 17.

B. Biosimilars are governed by a legal regime comparable to, but with notable distinctions from, the Hatch-Waxman Act.

Biosimilars are governed by a legal framework that, in many respects, parallels the framework under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act) that governs chemical generics, and patent litigation under each regime proceeds in a similar manner. But there are several important and relevant differences.

1. In 2010, Congress passed and the President signed the Biologics Price Competition and Innovation Act (BPCIA) to accelerate access to affordable biopharmaceuticals. *See generally* 42 U.S.C. § 262(k)-(*l*); *Sandoz*, 137 S. Ct. at 1669; *see also* 155 Cong. Rec. S7335, S7336 (July 10, 2009) (Statement of Sen. Sherrod Brown) ("Health care reform must broaden access to generic alternatives to biologics, the most expensive kinds of prescription drugs."). The BCPIA creates an abbreviated pathway for FDA approval of biosimilar products similar to the pathway that the Hatch-Waxman Act provides for generic chemical drugs, building on FDA's "longstanding policy of permitting appropriate reliance on what is already known about a drug, thereby saving time and resources and avoiding unnecessary duplication of human or animal testing." U.S. Food & Drug Admin., Implementation of the Biologics Price Competition and Innovation Act of 2009, https://bit.ly/318DmZW.

The BPCIA's abbreviated biologics license application (aBLA) process parallels the Hatch-Waxman Act's abbreviated new drug application (ANDA) process. Following an exclusivity period for any

approved biologic, a manufacturer of a new biopharmaceutical may gain FDA approval for the new drug by demonstrating that it is biosimilar to the reference biologic just as a generic manufacturer can gain FDA approval for a new chemical pharmaceutical by demonstrating that it is bioequivalent to an approved reference chemical drug. *See Sandoz*, 137 S. Ct. at 1670; *see also* 42 U.S.C. § 262(k). To obtain such approval, a biosimilar company "must show that its product is 'highly similar' to the reference product and that there are no 'clinically meaningful differences' between the two in terms of 'safety, purity, and potency.'" *Sandoz*, 137 S. Ct. at 1670 (quoting 42 U.S.C. §§ 262(i)(2)(A), (B)).

As in the chemical pharmaceutical context, FDA must approve biosimilar labeling. *See* 42 U.S.C. § 262(a)(2)(D); 21 C.F.R. § 201.100. "FDA regulations . . . require that prescription drug labeling [including biosimilar labeling] contain: 'adequate information . . . including indications, effects, dosages, routes, methods, and frequency and duration of administration and any relevant warnings, hazards, contraindications, side effects, and precautions, under which practitioners licensed by law to administer the drug can use the drug safely and for the purposes for which it is intended.'" U.S. Food & Drug Admin., Center for Biologics Evaluation & Research, Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed, Draft Guidance at 6 (Feb. 2020), https://bit.ly/3SFJa9n (quoting 21 C.F.R. § 201.100(d)(1)) (2020 FDA Draft Carve-Out Guidance).

Moreover, as with generic chemical pharmaceuticals, biosimilars may only be licensed for conditions that have been previously indicated for the reference product. *See* 42 U.S.C. § 262(k)(2)(A)(i)(II); *see* also 2020 FDA Draft Carve-Out Guidance at 3. But as under Hatch-Waxman, an aBLA "applicant generally may obtain licensure of a proposed biosimilar product for fewer than all conditions of use for which the reference product is licensed." U.S. Food & Drug Admin., Center for Biologics Evaluation & Research, Questions and Answers on Biosimilar Development and the BPCI Act, Guidance for Industry at 7 (Sept. 2021), https://bit.ly/3QySJou. The BPCIA thus similarly allows biosimilars to "carve out" indications from their labels that are still subject to patent protection, leaving only one or more unpatented indications on the label. *See* 42 U.S.C. § 262(k)(2)(A)(i)(III).

FDA has advised biosimilar companies how to develop a draft label that carves out patented uses of a biologic (*i.e.*, a skinny label). Specifically, FDA advises that "[t]he applicant should develop draft labeling for the proposed biosimilar or proposed interchangeable biosimilar that includes information from the reference product labeling that is relevant to the proposed conditions of use for the proposed biosimilar or interchangeable, *with appropriate modifications*. In preparing such draft labeling, the applicant should carefully scrutinize the content of all sections of the labeling to ensure that relevant information is included, *based on the proposed conditions of use* for the proposed biosimilar or interchangeable product. [Then,] FDA will evaluate the labeling to determine whether it complies with applicable requirements." 2020 FDA Draft Carve-Out Guidance at 5-6 (emphases added).

2. Despite these similarities, the two statutory and regulatory schemes—and the procedures under those schemes for coordinating the launch of new drugs and any patent litigation—also diverge in important respects.

First, the Hatch-Waxman Act imposes public disclosure requirements on branded chemical pharmaceutical companies that the BPCIA does not impose on branded biologic manufacturers.

As the petition explains, under Hatch-Waxman, a branded pharmaceutical company seeking FDA approval must declare all patents (except manufacturing-process patents) that cover their branded drug and its indications, along with a corresponding use code. *See* Pet. 8 (citing 21 U.S.C. § 355(b)(1)(A)(viii); 21 C.F.R. § 314.53(c)(2)(ii)(P)(3)). The branded company must submit a declaration, under penalty of perjury, to FDA that identifies each method of use and related patent claim covering its drug, as well as shorter use codes to describe the claimed method, *see* 21 C.F.R. § 314.53(c)(2), which FDA then makes publicly available in the so-called "Orange Book." 21 C.F.R. § 314.53(e). A generic manufacturer preparing an ANDA can then rely on those listings to know which patents the branded company believes claims an approved indication. *See* Pet. 8.

The BPCIA does not enforce the same requirements on branded biologic manufacturers, and thus biosimilars do not enjoy the same transparency in assembling an aBLA. In particular, under the BPCIA, there is no provision mandating that a biologic manufacturer seeking FDA approval of a new biologic to identify, or swear under the penalty of perjury as to, the patents that the manufacturer considers as

protecting the biologic or its on-label indications. As a result, biosimilar manufacturers largely rely on their own searches to determine the existing patent landscape for a reference biologic before submitting an aBLA and proposed label to FDA. In some instances, the biosimilar manufacturer may rely on a biologic's previous assertions about the patents that the biologic believes covers a different, previous biosimilar applicant for the same reference drug—which FDA publishes in what it calls the "Purple Book." *See* 42 U.S.C. § 262(k)(9); U.S. Food & Drug Admin., Purple Book Database of Licensed Biologic Products: Frequently Asked Questions with Answers, https://bit.ly/3p7zpTv. But even then, the listings are specific to the previous applicant and may not cover aspects of the subsequent biosimilar.

Second, the BPCIA provides an opportunity to engage in a prelitigation (and private) information-exchange between the biosimilar and the biologic manufacturer colloquially referred to as the "patent dance" intended to streamline or narrow the issues for litigation and to facilitate a biosimilar manufacturer's decision whether to launch at-risk and any related patent litigation alongside that launch. *See* 42 U.S.C. § 262(*l*)(3)-(6), (9).

The patent dance kicks off when the biosimilar company provides the reference biologic manufacturer with a copy of the aBLA along with other information describing the manufacturing process of the biosimilar at issue. *See* 42 U.S.C. § 262(*l*)(2); *see also Sandoz*, 137 S. Ct. at 1670-71. "After the applicant makes the requisite disclosures, the parties [then] exchange information to identify relevant patents and to flesh out the legal arguments that they might raise in future

litigation." *Sandoz*, 137 S. Ct. at 1671; *see* 42 U.S.C. § 262(*l*)(3).[2]

The purpose of this exchange is to narrow the issues for future litigation, not to complicate them. As this Court emphasized, "[t]he BPCIA sets forth a carefully calibrated scheme for preparing to adjudicate, and then adjudicating, claims of infringement." *Sandoz*, 137 S. Ct. at 1670.

Third, the two statutes and corresponding regulations establish different regimes for any associated patent litigation.

As the petition describes, the Hatch-Waxman Act requires that a generic manufacturer certify that it intends to follow one of three pathways to launch its drug. *See* Pet. 5-7. The generic manufacturer is required to indicate in its ANDA whether it will (1) wait to launch until all Orange-Book-listed patents covering the drug expire; (2) certify to FDA that the listed patents held by the brand manufacturer are invalid or will not be infringed by the generic launch; or (3) where the drug molecule itself is off-patent, submit a "section viii" statement that it will launch with a skinny label that carves out any patented on-label indications. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV), (viii); *see also* Pet. 6-7. If the generic manufacturer asserts patent invalidity or non-infringement, the

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[2] Since December 2020, the reference manufacturer must also provide to FDA the same list of patents it might raise in future litigation against the biosimilar, which FDA publishes in the "Purple Book." *See* 42 U.S.C. § 262(k)(9)(A)(iii); *see also* U.S. Food & Drug Admin., Purple Book Database of Licensed Biologic Products: Frequently Asked Questions with Answers, https://bit.ly/3p7zpTv.

Hatch-Waxman Act provides for an automatic 30-month stay of the regulatory approval process, pending the outcome of litigation (assuming certain conditions are met). *See* 21 U.S.C. § 355(j)(5)(B)(iii); *see also* Pet. 6.

By contrast, the BPCIA does not impose any automatic stay of the regulatory approval process for an at-risk launch. Pre-launch litigation can begin during the application process, *see* 42 U.S.C. § 271(e)(2)(C)(i) (making submission of an application for approval an act of patent infringement), and at the conclusion of any patent dance, the BPCIA "channels the parties" into litigation. *Sandoz*, 137 S. Ct. at 1671; *see id.* at 1671-72. But FDA may approve the biosimilar while the manufacturers continue to engage in negotiation or litigation, and upon receiving approval, the biosimilar may then launch without regard to the status of those negotiations or litigation.

3. Despite the distinctions between how small and large molecules get into patent litigation, once there, such disputes proceed in a similar manner, including the standard of proof. To prove that a biosimilar manufacturer has induced infringement of a reference biologic manufacturer's patent claim covering a method of using that biologic, the biologic company must demonstrate (1) direct infringement by another (*i.e.*, that a doctor or patient directly infringed the method of use) that was (2) knowingly aided and abetted by affirmative steps taken by a biosimilar to encourage direct infringement with (3) the affirmative intent that the product be used to infringe. *See Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 760 (2011).

To establish liability for induced infringement under Section 271(b) of the Patent Act for a product with

both patented and unpatented uses, it has long been understood that only "[e]vidence of active steps . . . taken to encourage direct infringement, such as advertising an infringing use or instructing how to engage in an infringing use, show an affirmative intent that the product be used to infringe," and that only "a showing that infringement was encouraged 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) (internal quotations marks and citations omitted). Mere mention or description of a potentially patented use is not sufficient; one must recommend, promote, or encourage a patented use, or suggest that a patented use should be performed. *See Global-Tech Appliances*, 563 U.S. at 760.

In the pharmaceutical context, the Federal Circuit has thus made clear that, to induce infringement of a drug with both patented and unpatented on-label indications, an allegedly infringing drug's label must "encourage, recommend, or promote infringement." *Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015). Particularly "in the Hatch-Waxman context . . . designed to enable the sale of drugs for non-patented uses," the court determined that "vague label language cannot be combined with speculation about how physicians may act to find inducement." *Id.* at 631-32.

Although the Federal Circuit panel did not purport to change this well-settled law, the result of its decision threatens to undermine Congress's carefully calibrated scheme to encourage competition among pharmaceuticals.

II. The Federal Circuit's Decision Poses a Heightened Threat to Congress's Procompetitive Statutory Scheme for Biosimilars.

The Federal Circuit's decision provides branded companies an unwarranted new tool in their efforts to prevent or delay competition, whether generic or biosimilar. And the differences between the regimes governing biosimilars and generics may exacerbate the harm with respect to access to biosimilars in a manner that fundamentally disrupts the BPCIA's statutory design.

A. As the petition explains, the Federal Circuit's decision will likely be used by branded pharmaceutical companies in an effort to blur the lines between infringing and non-infringing conduct and to dilute the evidentiary showing of intent and affirmative encouragement required to impose liability for induced infringement in the context of pharmaceuticals.

In the decision below, the Federal Circuit upheld an inducement verdict based on unconnected piecemeal statements in an FDA-approved label and a disparate collection of what would otherwise be non-infringing, truthful statements from various points in time, across several documents, about unpatented uses. *See* Pet. App. 15a-17a (relying on, *e.g.*, the indication for an unpatented use, the dosage section, and the clinical studies section of the FDA-approved label); *id.* at 31a-32a (relying on product materials accurately describing FDA's anticipated and eventual approval). And the result—a nearly $235 million jury verdict more than three times *all* of petitioner's sales for *all uses* during the relevant period, *see id.* at 43a; *id.* at

123a n.3 (Prost, C.J., dissenting)—is too simply much to expect brand manufacturers to ignore.

Although Alvotech takes the Federal Circuit at its word that, even after the decision below, "generics [can]*not* be held liable for merely marketing and selling under a 'skinny' label omitting all patented indications, or for merely noting (without mentioning any patented uses) that FDA had rated a product as therapeutically equivalent to a brand-name drug," Pet. App. 11a, the petition rightly observes that if brand manufacturers need "only to find claim elements 'mentioned' in portions of [a generic's] label that speaks to *unpatented* uses, [they] will regularly find *something* in the skinny label that can serve as the basis for an inducement complaint years (and hundreds of millions of dollars) after generic launch." Pet. 33.[3]

The threat of devastating liability if a jury gets it wrong threatens to upset the careful balance that Congress struck in *both* the Hatch-Waxman Act and the BPCIA to protect innovation while recognizing the clear benefits of accelerating the introduction of competition to market. And the risk of such ruinous litigation will loom large in the decision about when and whether to launch new biosimilars, just as it does generics. The consequence will be fewer generic and

[3] Indeed, the decision will encourage branded manufacturers to, as one FDA attorney recently put it, develop strategies for "structur[ing] their own labeling so that they have a 'better chance of success in future skinny label cases,' " such as by "seed[ing] potentially problematic language" in parts of their label with the intention that, when copied to a generic's label, it will create grounds for future inducement liability. Ian Lopez, *Hikma Drug Label Win Still Leaves Generics on Hook for Liability*, BLOOMBERG LAW (Jan. 12, 2022), https://bit.ly/3Qk1dQF.

biosimilar launches, less competition, and fewer consumer health benefits.

B. Because biosimilars are governed by a similar legal regime, the Federal Circuit's decision is at least as problematic for biosimilars as chemical generics. Indeed, several differences between the markets for chemical drugs and biopharmaceuticals and between the BPCIA and Hatch-Waxman regimes could amplify and compound the harm of the decision below.

First, because of the relative differences in market size between small-molecule drugs and large-molecule drugs, the Federal Circuit's decision is likely to have a disparate impact on biosimilars as compared with small-molecule drugs. As discussed in Section I.A, *supra*, the average price of biologics is several times that of their small-molecule counterparts. *See* Andrew Mulcahy et al., *Biosimilar Cost Savings in the United States: Initial Experience and Future Potential*, 7(4) RAND HEALTH Q. 3 (2018). The potential jury verdicts, including lost profits or treble damages, that could result from an at-risk biosimilar launch are therefore significantly greater for biosimilar companies than their generic drug counterparts. *See* Pet. App. 42a-45a (affirming an award of lost profits for the branded company). And thus the incentives to avoid such liability by avoiding such an at-risk launch may be all the greater until a court has rejected a lawsuit like this one, providing the biosimilar greater certainty that courts will find its label "skinny enough."

Second, the Federal Circuit's decision is likely to exacerbate harm caused by certain other patent practices that are particularly prevalent among biopharmaceuticals. The federal government has already identified "patent thickets" as an impediment to

competition, particularly in the biologic space. *See generally* Cong. Research Serv., *Drug Pricing and Pharmaceutical Patenting Practices* 16, 24 (2020), https://bit.ly/3Qsi1EY (*Patenting Practices*); *see also* Sen. P. Leahy Ltr. to Hon. K. Vidal (June 8, 2022), https://bit.ly/3JLripi (explaining that branded companies attempt to threaten competitors with larger patent portfolios by filing numerous, overlapping patents that relate to or cover the same invention). This problem only stands to be exacerbated by the Federal Circuit's decision, which encourages brand companies to expand the patent thickets with multiple method-of-use patents claiming off-label uses in the hopes that they can find some language in the labeling to justify an inducement claim.

The threat of costly patent litigation in which tens of patents, hundreds of patent claims, and millions upon millions in damages may be brandished against biosimilar manufacturers—*i.e.*, ruinous litigation—is already enough to postpone otherwise apt competition from entering the market or coercing them to settle. *See Patenting Practices* 26-27 (noting that Johnson & Johnson has over 100 patents covering its autoimmune disorder drug Remicade® and Biogen/Genentech filed 204 patent applications to protect cancer treatment Rituxin®). The problem will only be made worse if branded companies are permitted to rely on the decision below to establish inducement of their ever-expanding thicket of off-label, method-of-use patents.

Third, the different disclosure requirements for branded manufacturers under the BPCIA is likely to increase the harm to biosimilar companies from the decision below. As noted, unlike the Hatch-Waxman

Act, neither the BPCIA nor biopharmaceutical regulations require branded biologic companies seeking FDA approval to list the non-process patents that cover a branded drug and its indications for use in a public database like the Orange Book. Thus, while generic chemical drug companies "can rely on what brands say their patents cover" when they draft their carveout labels, Pet. App. 52a (citing *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 407 (2012)), biosimilar companies do not necessarily enjoy the same privilege.

The different disclosure regime may carry both practical and legal consequences. As a practical matter, it deprives biosimilar manufacturers of the advance notice provided by the Orange Book of the brand's view of the relevant patents that *could* be asserted even against a skinny label—making it only more difficult to craft one adequate to avoid litigation. It is not until the patent dance, after the biosimilar's aBLA application has been accepted by FDA, that the biosimilar company is provided with a list of patents that the branded biologic alleges is infringed by the biosimilar's proposed labeling. And while some second or subsequent biosimilar applicants may be able to rely in part on listings in the Purple Book (if the previous applicant engaged in the patent dance), those listings are specific to the previous biosimilar applicant's label, and so may not directly apply. *See* Evan Diamond et al., *"Purple Book" Patent Listing Under Biological Product Patent Transparency Act*, J.D. SUPRA (Apr. 8, 2021), https://bit.ly/3bIi0xX.

In addition to those practical difficulties, the lack of an advance declaration by the brand, under penalty of perjury, further complicates the possibility that

equitable estoppel could mitigate the effects the Federal Circuit's decision for biosimilars. Biosimilars would not have the same basis for appealing to the discretionary equitable-estoppel doctrine that some members of the Federal Circuit suggested might serve as an answer to the problems caused by the Federal Circuit's decision. *See* Pet. App. 190a-93a (Moore, C.J., concurring) (suggesting that equitable estoppel might mitigate the harm of the decision for generic chemical drug manufacturers); *see also* Pet. 36-37.

C. The potential harm from the decision on the biopharmaceutical market is even more problematic when one considers how it disrupts the design innovations of the BPCIA (1) to streamline litigation using a patent dance, and (2) to permit more at-risk launches than the Hatch-Waxman Act allows.

First, the BPCIA's patent dance is a departure from Hatch-Waxman certification procedures designed to streamline patent litigation concerning a new biosimilar. The biosimilar manufacturer privately shares information with the branded manufacturer, enabling the parties to negotiate or focus any litigation concerning the launch. The decision below, however, threatens to disrupt that streamlined process by encouraging brand companies to use the patent dance to list numerous off-label, method-of-use patents, arguing there is enough from the label to assert in litigation. Instead of serving as a tool to streamline litigation, the patent dance could become simply another means to complicate it and create uncertainty for the biosimilar manufacturer.

Second, the BPCIA departed from Hatch-Waxman to more often permit at-risk launches of biosimilars. As discussed above, unlike the Hatch-Waxman Act,

the BPCIA never imposes an automatic stay of the approval process for an at-risk launch, encouraging biosimilars to launch more quickly even while litigation is ongoing (subject only to the possibility of an injunction). *See* p. 14, *supra*. By substantially increasing the potential cost of an at-risk launch, however, the Federal Circuit's decision threatens to negate Congress's decision—by effectively imposing the same barrier to an accelerated launch through increased litigation risk.

III. Limiting Consumer Access to Biosimilars Would Have Dire Consequences for Public Health.

If left undisturbed, the Federal Circuit's decision threatens to have adverse impacts on the public health and welfare of the United States through decreased competition, increased prices of already-expensive pharmaceuticals, and, ultimately, reduced patient access to life-saving medications.

First, the decision may lead to decreased competition not only in the chemical pharmaceutical market but also in the biologic space. At a minimum, expanded threatened or actual litigation may have a chilling effect in the number of biosimilars that decide to come to market only after a district court has rejected the biologic's claims of induced infringement based on a lawful skinny label. And that chilling effect may be compounded by a reference biologic company's efforts to expand patent thickets around their branded products with off-label, method-of-treatment patents that they hope to convince a court or jury that words somewhere in the biosimilar's labeling infringe.

Second, the lower court's opinion may also lead to higher biopharmaceutical product prices overall, both on the branded side and biosimilar side. In the absence of robust competition, biologics companies can be expected to continue to inflate the prices of their drugs, costing patients and the federal government billions of dollars, and contributing to the drug-pricing crisis. *See* STAFF OF H. COMM. ON OVERSIGHT & REFORM, 117th Cong., Drug Pricing Investigation AbbVie—*Humira and Imbruvica* at i (Staff Rep. May. 2021), https://bit.ly/3C14mkf (describing AbbVie's "uninhibited price increases" for its biologics, including a 470% increase for Humira since its 2003 launch). One former FDA Commission estimated that delays in biosimilar entry to market caused by anticompetitive strategies like patent abuse already cost Americans more than $4.5 billion in 2017 alone. *See* Remarks from FDA Commissioner Scott Gottlieb, M.D., as prepared for delivery at the Brookings Institution on the release of FDA's Biosimilars Action Plan (July 18, 2018), discussed in *Failure to Launch: Patent Abuse Blocks Access to Biosimilars for America's Patients*, BIOSIMILARS COUNCIL 6 (June 2019), https://bit.ly/3SA6NA7.

Moreover, if biosimilar companies are threatened with ruinous litigation, it would be infeasible not to incorporate such litigation costs into the price of biosimilars. In this case, the Federal Circuit affirmed a verdict of nearly $235 million dollars against petitioner for induced infringement of respondents' method-of-use patent. Pet. App. 43a-45a. As noted, petitioner made only $74.5 million in all of its sales of the generic during the period-in-question. *See* Pet. 12. Thus, "it was ultimately more costly for [petitioner] to sell an unpatented drug for unpatented uses than it

would have been to stay out of the market altogether." Pet. App. 145a-46a (Prost, C.J., dissenting). The economics are not any better in the biosimilar markets; in fact, they are far worse. As discussed, large molecule biopharmaceuticals can be up to twenty times the price of small molecule drugs; thus, lost-profit damages can be significantly higher. These potentially debilitating verdicts could deter biosimilars from launching at risk. *See, e.g.*, *Amgen Inc. v. Hospira, Inc.*, 944 F.3d 1327, 1340-41 (Fed. Cir. 2019) (affirming a $70 million infringement verdict based on pre-launch batches not subject to a safe harbor).

Finally, both depressed competition and increased drug prices will ultimately lead to reduced patient access to necessary medications. Without the ability for biosimilars to predictably determine what to include in their carveout labels to avoid threatened or actual induced infringement litigation and to accurately judge the risk of an at-risk launch, the drug-pricing crisis America faces is poised to worsen. For many Americans who cannot afford these increases, more and more will lose the ability to afford the medications and care they need. The U.S. healthcare system and the American people cannot afford that outcome.

CONCLUSION

For the foregoing reasons, the petition for a writ of certiorari should be granted.

Respectfully submitted,

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