Appeal Nos. 2018-1976, 2018-2023

IN THE

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

GLAXOSMITHKLINE LLC, SMITHKLINE BEECHAM (CORK) LIMITED,

Plaintiffs-Appellants,

v.

TEVA PHARMACEUTICALS USA, INC.,

Defendant-Cross-Appellant.

Appeal from the United States District Court for the District of Delaware in Case No. 1:14-cv-00878-LPS-CJB

Chief District Judge Leonard P. Stark

BRIEF OF KNOWLEDGE ECOLOGY INTERNATIONAL AND JAMES PACKARD LOVE AS AMICI CURIAE

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Dated: December 16, 2020

CERTIFICATE OF INTEREST

Case Number: 18-1976, 18-2023

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

Filing Party/Entity: Knowledge Ecology International and James Packard Love

Pursuant to Federal Circuit Rule 47.4, I hereby certify the following:

(1) The full name of the *amicus* represented by me in this case is:

Knowledge Ecology International and James Packard Love.

(2) The name of every real party in interest represented by me in this case is:

None.

(3) For each entity represented by me, the parent corporations of such entity and every publicly held corporation that owns ten percent or more of such entity's stock are: **None.**

(4) The name of all law firms and the partners or associates that appeared for the party or amici now represented by me in the trial court or are expected to appear in this Court (and who have not or will not enter an appearance in this case) are: **Kathryn Ardizzone, Knowledge Ecology International, Washington, D.C.**

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

(6) All information required by Federal Rule of Appellate Procedure 26.1(b) and (c) that identifies organizational victims in criminal cases and debtors and trustees in bankruptcy cases is: **None.**

Dated: December 16, 2020

/s/ Kathryn Ardizzone
Kathryn Ardizzone

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INTEREST OF *AMICI CURIAE*

Knowledge Ecology International ("KEI") is an international non-profit, non-governmental organization that searches for better outcomes, including new solutions, to the management of knowledge resources. In particular, KEI is focused on the management of these resources in the context of social justice. KEI is drawn to areas where current business models and practices by businesses, governments or other actors fail to adequately address social needs or where there are opportunities for substantial improvements. KEI has expertise on issues pertaining to intellectual property and medical technologies, among other fields.

James Packard Love is the director of KEI, and a consultant and advisor to several governments, UN agencies and non-government agencies.

James Packard Love and KEI are interested in this petition for rehearing *en banc* because the precedent set by this case will have enormous consequences for the affordability of medical inventions.

SUMMARY OF THE ARGUMENT

The Panel's decision expands the doctrine of induced infringement, making it easier for a party to satisfy their burden of persuasion when alleging induced infringement against a company that markets a generic product for use in a non-patented indication.

The dissent suggests that the Panel's decision, although incorrect, was motivated by a desire to incentivize companies to undertake research on new uses of medical products that have been approved by the United States Food and Drug Administration (FDA) for other uses. We argue that while patents provide an incentive for investments in research on new uses, the patent system is poorly designed for such a purpose, and may provide either excessive or inadequate protection for new uses.

Courts should be aware that the enforcement of patents on new uses is only one of many mechanisms that are available to directly fund, subsidize or reward such investments, and not the most efficient, in this case creating a deep and consequential conflict between innovation incentives on the one hand, and affordability and access to unpatented inventions on the other.

The Panel need not be concerned that sustaining the decision of the United States District Court for the District of Delaware granting judgment as a matter of law to Defendant-Cross-Appellant Teva Pharmaceuticals USA, Inc., might jeopardize future investments in research on new uses of older medicines. Absent the Panel's expansion of the tort of induced patent infringement, policymakers can continue to use existing mechanisms to fund, subsidize and reward such research, or create new tools, as needed.

Accordingly, the Court should grant rehearing *en banc* and revisit the issues at hand with a new lens.

ARGUMENT

I. EXPANDING PATENT PROTECTION ON NEW USES OF OLDER MEDICINES THROUGH THE DOCTRINE OF INDUCED INFRINGEMENT IS COSTLY, CONFLICTS WITH OTHER OBJECTIVES REGARDING ACCESS TO AND AFFORDABILITY OF OLDER MEDICINES, AND IS UNNECESSARY WHEN OTHER MECHANISMS TO DIRECTLY FUND, SUBSIDIZE AND REWARD RESEARCH ON NEW USES OF OLDER MEDICINES ARE MORE EFFICIENT.

Chief Judge Prost's dissent in the operative opinion describes the broader conflicts courts seek to balance when deciding complex patent disputes such as the case at bar:

> Through the decades, many, including my colleagues, have spoken on the importance of patents in incentivizing innovation. The calls for robust patent protection have been particularly passionate in the pharmaceutical space. The critical balance of those patent rights, however, is public access to the innovation once patents have expired. Indeed, Congress designed the generic approval system with the express purpose of speeding the introduction of generic drugs to the market as soon as patents allow. Today, the Majority's decision undermines this balance by allowing a drug marketed for unpatented uses to give rise to liability for inducement and by permitting an award of patent damages where causation has not been shown.

GlaxoSmithKline LLC v. Teva Pharm. USA, Inc., 976 F.3d 1347, 1356 (Fed. Cir. 2020) (Prost, C.J., dissenting).

The primary justification for patenting new uses for an older drug is to stimulate investment in human clinical trials. These trials can be costly, require investments, and involve the risk of failure.

Patents granted for a method of use that describes a new indication for an older drug, can, in theory, be used to provide commercial benefits to investors in such trials. In

practice, however, the patent system is at best an awkward and imperfect incentive mechanism for the new use patents. Depending upon the application of different enforcement methods, protection can either be excessive or inadequate, even when courts attempt to strike a middle ground.

The challenge in using the patent system to induce investments in research on older drugs can be illustrated by considering the case in which a drug has two approved uses, one older and now off-patented use, and another use covered by the new method-of-use patent—two polar extremes that illustrate the range of outcomes that investors, competitors and courts confront. If a less expensive generic drug can be placed on the market for the older use, and then freely used by patients for both indications, the patent on the new use is no longer effective in providing the benefit of a monopoly (at least for the period following the expiration of the original patent).

If a company that markets a generic drug for an older, off-patent indication is subject to ruinous damages when the product is purchased by patients for the patented new use, this can have the effect of chilling competitors' willingness to manufacture a generic equivalent for off-patent uses and extend the monopoly for the original older use.

Courts have sought to manage this conflict by creating a set of rules governing instances in which the marketing of generic products creates an inducement to infringe. The market for drugs approved by the FDA makes this approach particularly challenging, as both a brand-name and generic products will have the same International Nonproprietary Name. This challenge is compounded by the fact that when the FDA grants an Abbreviated New Drug Application (ANDA), it certifies that drugs are

bioequivalent, and effectively the same medically, while prices are typically radically different.

If courts rely upon aggressive arguments about technically obscure nuances in providing information about drugs to physicians or the public for determining causation of infringement, courts are effectively suggesting that physicians and patients are surprisingly ignorant when it comes to understanding the substitutability of products the government has determined, in publicly available documents, to be equivalent. In the age of internet-accessible information about medicines, from *Wikipedia* to the FDA's own webpages, this is a fragile mechanism.

For society, it is fortunate that the patent system is only one of many tools to advance investments in research.

II. CONGRESS HAS ENACTED OR PROPOSED MORE EFFECTIVE, LESS COSTLY MECHANISMS FOR ADVANCING RESEARCH

For drugs more so than for most products, Congress has enacted an impressive set of mechanisms to directly fund, subsidize, and reward investments in biomedical research, outside of the patent system. Some of these mechanisms are clearly designed to provide protections in areas where patents for inventions are not available or otherwise offer inadequate protection for investments. Below, we discuss some of these non-patent mechanisms, including those that mimic the patent system by providing some measure of exclusive rights, and others that do not rely upon the prospect of a monopoly as an incentive. In each of these selected examples, Congress has found or considered practical

solutions to overcome perceived limits to the patent system for advancing biomedical research and development.

A. Various laws authorize the FDA to stimulate investment in biomedical development.

For drugs, FDA approval provides sponsors exclusive rights to the data used to establish safety and efficacy, for both new products and new uses for existing products. For a drug registered under a New Drug Application (NDA), this regulatory benefit confers five years of exclusive rights in the data used to register a new drug and three years of exclusive rights in the data used to support the expansion of a marketing approval for new indications for an existing drug. 21 U.S.C. § 355(j)(5)(F)(iii)-(iv)). For biologic products, FDA approval of a biosimilar product provides a similar but somewhat different set of rights in data on the safety and efficacy of a reference product. 42 U.S.C. § 262(k)(7). Exclusive rights to rely upon regulatory test data are similar to patent rights in the sense they are designed to create barriers to the entry of a generic or biosimilar competitor.

The Orphan Drug Act (ODA), 21 U.S.C. § 360aa–360ee, provides for several different regulatory benefits and incentives designed to induce investment in research and development for treatments for orphan diseases, including new uses of older drugs, for a "rare disease". The benefits and incentives under the ODA include "Grants and contracts for development of drugs for rare diseases and conditions," reduced regulatory fees (21 U.S.C. § 360ee), a twenty-five percent tax credit applied to the cost of qualifying clinical

trials (26 U.S.C. § 45C), and a regulatory monopoly of seven years for a specific orphan indication (21 U.S.C. § 360cc).

The FDA is also authorized to grant drug manufacturers a six-month extension of exclusivity in patents, test data and orphan drug exclusivity, to induce investments in clinical trials involving pediatric patients. Under 21 U.S.C. 355a, the FDA may issue a written request to the holder of an NDA to investigate their product in children. If the NDA holder conducts the trial and the FDA accepts the results, the NDA holder is entitled to an additional six-month period in which the FDA is prohibited from approving Abbreviated New Drug Applications (ANDAs) submitted by generic manufacturers. 21 U.S.C. § 355a(b)-(c). This program has been criticized for providing excessive benefits to drug companies, because the profits from and the costs to the patients of the patent extensions often far exceed the costs of the relatively small and often inexpensive pediatric trials. *See generally*, Michael S. Sinha, Mehdi Najafzadeh, Elizabeth K. Rajasingh, James Love, Aaron S. Kesselheim, *Labeling Changes and Costs for Clinical Trials Performed Under the US Food and Drug Administration Pediatric Exclusivity Extension, 2007 to 2012*. 178 JAMA INTERN MED 1451-1466 (2018), *available at* doi:10.1001/jamainternmed.2018.3933.

In the *JAMA Internal Medicine* article cited above, the authors suggest that the federal government replace the grant of the extended monopoly with a system of cash payments or directed research:

> If policymakers determine that the costs to consumers for pediatric exclusivity extensions described in the present study are excessive, an alternative would be to set a fixed or predetermined award amount for each

> requested study, claimable on successful completion of pediatric studies. Such an approach would not require companies to wait several years to recoup capital invested in pediatric research, and it would be less expensive for the public, particularly for products with substantial revenues, in which the extension of the monopoly creates the largest mismatch between the incentive and the cost. Another approach would be direct funding of pediatric trials through the National Institutes of Health (NIH). This could include increased allocations to the Pediatric Trials Network, which is funded by the NIH's National Institute of Child Health and Human Development. Because government-sponsored prescription drug insurance programs cover more than 100 million patients, taxpayers already bear a substantial proportion of the costs associated with delayed availability of generic drugs. Federal funding could also expand the scope of studies to include pediatric uses of drugs that are already generic but continue to be prescribed to children without the necessary data. The NIH already publishes a Priority List of Needs in Pediatric Therapeutics for use in this line of research.

Id. at 1464 (internal citations omitted).

FDA "priority review vouchers" (PRVs) are mechanisms to stimulate investment in the development of treatments for neglected diseases or to encourage development of treatments for rare pediatric diseases. 21 U.S.C. § 360n; 21 U.S.C. § 360ff. The PRV is an example of an incentive that does not involve the grant of a monopoly. The vouchers allow a company to obtain accelerated approval for a drug or biological product that otherwise is not entitled, and this may shorten the time for regulatory review by roughly a half year. *See* https://priorityreviewvoucher.org/. PRVs are also saleable, 21 U.S.C. § 360n(b)(2) and 21 U.S.C. § 360ff(b)(2), and are often sold to companies seeking to accelerate market entry for diseases that are expected to have large markets. When traded, PRVs can be sold for high prices and have recently been sold for roughly $100 million. *See* https://priorityreviewvoucher.org/.

Congress initially enacted the PRV system in 2007 under the Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 1102, 121 STAT 825, 972-74 (2007), motivated by the academic article, David B. Ridley et al., *Developing Drugs for Developing Countries*, 25 HEALTH AFF. 313 (2006). https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.25.2.313. In 2012, largely due to the advocacy efforts of Nancy Goodman and her non-profit group, Kids v Cancer, *see* Nancy Goodman, *How the RACE for Children Act will get drugs to kids with cancer*, September 8, 2017. THE CANCER LETTER, https://cancerletter.com/articles/20170908_2, Congress extended the PRV to "the prevention or treatment of a rare pediatric disease", *see* the Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. No. 112-144 § 908, 126 STAT. 995, 1094-98 (2012), codified at 21 U.S.C. § 360ff.

Among these current mechanisms to induce investment in research and development, there is considerable diversity in the approaches, on such dimensions as the reliance upon exclusive rights, the sharing of risks, and the magnitude of the costs to consumers and benefits to drug companies.

B. Members of Congress have proposed legislation to require or evaluate the use of cash rewards to induce pharmaceutical investment.

In recent years, there has been renewed interest in the use of innovation inducement prizes, including large market entry rewards (MERs), to reward successful development of new drugs, vaccines or diagnostic tests.

Bills have been introduced that propose implementing MERs in different forms. The Affordable Medications Act (S.1801), a bill introduced in the 116th Congress, proposed awarding pharmaceutical companies $2 billion in market entry rewards for the development of three new antibiotic drugs. S.1801, 116th Cong. § 301. One of the rationales for the use of MERs for antibiotic drugs is the conflict between the need to restrict access to the drug, in order to limit antibiotic drug resistance, and the company's incentive to sell the drug as widely as possible, as often as possible, during the period of the monopoly. The use of MERs is seen as allowing society to properly conserve the biologic resource for treating patients who need it the most, while providing robust incentives to drug developers.

Several members of Congress have also proposed that the National Academies of Sciences, Engineering and Medicine conduct a study to examine "the use of innovation inducement reward funds and push financing mechanisms as ways to stimulate investments in biomedical research and development that de-links costs from product prices." S.1801, 116th Cong. § 301(j).

C. The federal government and charities provide funding to support the clinical development of new uses for approved drugs.

In the case of new uses for approved drugs, the National Institutes of Health (NIH) and other federal agencies that sponsor biomedical research and development (R&D) have provided grants to fund clinical trials, and academic centers and patient groups have also often funded trials.

The federal government, charities, and other non-industry sources fund a significant proportion of clinical trials registered at ClinicalTrials.gov, an online database of clinical trial information maintained by the NIH and the National Library of Medicine. *See* NAT'L INSTITUTES OF HEALTH, NAT'L LIBRARY OF MEDICINE, *ClinicalTrials.gov Background*, https://clinicaltrials.gov/ct2/about-site/background. ClinicalTrials.gov allows users to search clinical trials by funder type: the U.S. government, industry and "other." The category "other" includes non-profit organizations such as universities or charities as well as foreign governments. According to a query of the database on December 15, 2020, there are 19,051 trials that are classified as interventional studies with results reported that have been completed, in Phase 2 or 3 (studies used to expand the label). Of these, 31 percent are funded by the "NIH", "Other Federal" or "Other".

NIH	2,934
Other Federal	355
Industry	13,534
Other	2,624.

Among these mechanisms to induce investment in research and development, there is considerable diversity in the approaches, on such dimensions as the reliance upon exclusive rights, the sharing of risks, and the magnitude of the costs to consumers and benefits to drug companies.

D. World Intellectual Property Organization study illustrates the rich diversity of tools used by policy makers.

The World Intellectual Property Organization (WIPO) is the specialized United Nations agency with the mission of "the development of a balanced and effective

international IP system that enables innovation and creativity for the benefit of all." *See* https://www.wipo.int//. WIPO administers a number of patent-related treaties, including the Paris Convention for the Protection of Industrial Property, the Patent Cooperation Treaty and the Patent Law Treaty, three treaties which the United States has joined. The Member States of WIPO asked the Secretariat to undertake a study of alternatives to the patent system to support of R&D efforts. The product of that study was *Alternatives to the Patent System that are used to Support R&D Efforts, Including both Push and Pull Mechanisms, with a Special Focus on Innovation-Inducement Prizes and Open Source Development Models*, CDIP/14/INF/12, September 14, 2014, World Intellectual Property Organization. This study surveyed a wide range of policy instruments to promote innovation, and illustratives the rich diversity of tools used by policy makers.

CONCLUSION

Courts have been asked to find ways to expand patent protection of new uses of older medicines, including those medicines with no patent protection. This task is fraught with challenges, due to the mismatch between the patent system and the competing policy objectives of rewarding one invention without creating barriers to competition and access to an earlier one. One strategy is to continually redefine and, in the hopes of the original monopolist, expand enforcement rights. But in the case of pharmaceutical drugs, policymakers have a set of options much broader than patent exclusivity to address such issues. Accordingly, in this case, the Panel should grant a rehearing *en banc* and analyze the legal issue at bar within the confines of current case law defining the parameters of induced infringement. Policymakers are best suited to continue to explore how best to

advance biomedical research without harms to competition, affordability and patient access to older drugs.

If the Panel's expansion of the doctrine of induced infringement in the case at bar relied upon concerns about providing robust patent enforcement to incentivize investment in new diseases indications, we respectfully submit that those concerns were either misplaced or given excessive emphasis.

We urge the court to grant the petition for rehearing *en banc* and analyze the issues at bar with the understanding that operating within the framework of the current jurisprudence on induced infringement rather than expanding it would not harm innovation on new disease indications.

Dated: December 16, 2020

Respectfully Submitted,

/s/ Kathryn Ardizzone

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CERTIFICATE OF COMPLIANCE

The foregoing filing complies with the relevant type-volume limitations of Federal Rule of Appellate Procedure 29(b)(4) and Federal Circuit Rule 35(g)(3) because it has been prepared using a proportionally-spaced typeface and includes 3088 words, exclusive of the parts exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2).

Dated: December 16, 2020

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