Nos. 2018-1976, 2018-2023

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.

On Appeal from the United States District Court for the District of Delaware
Chief District Judge Leonard P. Stark Case

No. 1:14-cv-00878-LPS-CJB

CORRECTED BRIEF OF *AMICI CURIAE* KNOWLEDGE ECOLOGY INTERNATIONAL AND JAMES PACKARD LOVE IN SUPPORT OF DEFENDANT-CROSS-APPELLANT'S PETITION FOR REHEARING *EN BANC*

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December 28, 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 *amici* 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: ***GlaxoSmithKline LLC v. Glenmark Pharmaceuticals Inc., USA*, No. 1:14-cv-877 (D. Del.).**

(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 28, 2020

/s/ Kathryn Ardizzone
Kathryn Ardizzone
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INTEREST OF *AMICI CURIAE*

Knowledge Ecology International (KEI) is a nonprofit organization that searches for better outcomes regarding the management of knowledge resources. James Packard Love is director of KEI. *Amici* are concerned this case will impact the affordability of medical inventions.

Amici curiae certify that no party's counsel authored this brief in whole or in part; no party's counsel contributed money intended to fund preparing or submitting this brief; and no person other than *amici curiae*, its members, or its counsel contributed money that was intended to fund preparing or submitting this brief. Pursuant to Rule 35(g), a motion for leave to file is being submitted.

SUMMARY OF ARGUMENT

The Panel's decision expands the doctrine of induced infringement against a company that appropriately marketed 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 Food and Drug Administration (FDA) for other uses. While patents provide an incentive for investments in research on new uses, they are poorly designed for such a purpose, and may provide either excessive or inadequate protection for new uses.

Enforcement of patents on new uses is only one of many mechanisms that are available to directly fund, subsidize or reward 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.

Affirming the verdict for Teva will not jeopardize future investments in research on new uses of older medicines. Policymakers can continue using 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.

ARGUMENT

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

The dissent in the operative opinion describes the broader conflicts courts seek to balance when deciding complex patent disputes:

> 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.

Dissent 21-22.

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

Patents granted for a method of use that describes a new indication for an older drug can 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 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 off-patented use, and another use covered by the new method-of-use patent—two different scenarios that illustrate the range of outcomes that investors, competitors and courts confront. If a cheaper 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 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 use, this can chill competitors' willingness to manufacture generic equivalents for off-patent uses and extend monopolies for original uses.

Courts have sought to manage this conflict by creating a set of rules governing instances in which marketing generic products induces infringement. 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. Furthermore, when the FDA grants an

Abbreviated New Drug Application (ANDA), it certifies that drugs are bioequivalent—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.

Fortunately for society, the patent system is only one of many tools to advance investments in research.

II. CONGRESS HAS ENACTED NON-PATENT MECHANISMS FOR ADVANCING RESEARCH.

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 are not available or otherwise offer inadequate protection for investments. Below, we discuss some of these non-patent mechanisms, including those that do not rely upon a monopoly. In each example, Congress has found

solutions to perceived limits to the patent system for advancing biomedical research and development (R&D).

A. FDA Subsidies and Incentives

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 biologics, FDA approval of a biosimilar 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 measures designed to advance research for orphan diseases, including new uses of older drugs. The benefits under the ODA include "Grants and contracts" (21 U.S.C. § 360ee), reduced regulatory fees (21 U.S.C. § 379h(a)(1)(F)), a 25-percent tax credit for 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 a six-month extension of exclusivity in patents, test data and orphan drug exclusivity, to induce investments in clinical trials involving pediatric patients. *See* 21 U.S.C. 355a. This program has been criticized for providing excessive benefits to drug companies, because the profits from and the costs to patients of the patent extensions often far exceed the costs of the relatively small and often inexpensive pediatric trials. *See generally*, Michael Sinha et al., *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 1458 (2018). The *JAMA Internal Medicine* authors propose replacing 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).

Id. at 1464 (citations omitted).

FDA "priority review vouchers" (PRVs) are a mechanism to stimulate investment in the development of treatments for neglected tropical diseases or rare pediatric diseases. PRVs do not involve a monopoly. They allow companies to obtain accelerated approval for a drug or biological product that otherwise is not entitled to it, *see* 21 U.S.C. § 360n (for tropical diseases); 21 U.S.C. § 360ff (for rare pediatric diseases), and this may shorten regulatory review by roughly six months, *see* https://priorityreviewvoucher.org/. PRVs are also saleable, and are often sold to companies seeking to accelerate market entry for diseases expected to have large markets. When traded, PRVs can be sold for high prices and have recently been sold for $100 million. *See id.*

Congress initially established the PRV system in 2007 under the Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 1102, 121 Stat. 823, 972-74 (2007), motivated by the academic article, David Ridley et al., *Developing Drugs for Developing Countries*, 25 HEALTH AFF. 313 (2006). In 2012, largely due to the advocacy efforts of Nancy Goodman, Congress extended the PRV to "the prevention or treatment of a rare pediatric disease". *See* Nancy Goodman, *How the RACE for Children Act will get drugs to kids with cancer*, THE CANCER LETTER (Sept. 8, 2017), https://cancerletter.com/articles/20170908_2 and Pub. L. No. 112-144 § 908, 126 Stat. 995, 1094-98 (2012).

Among these mechanisms to induce R&D investment, there is considerable diversity. None has a term of 20 years, some measures avoid monopolies altogether, and risk sharing varies.

B. Legislative Reform Proposals

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), for example, proposed awarding pharmaceutical companies $2 billion in MERS for the development of three new antibiotic drugs. S. 1801, 116th Cong. § 301. S. 1801 also proposed a study to examine "the use of innovation inducement reward funds and push financing mechanisms as ways to stimulate investments in biomedical R&D that de-links costs from product prices." *Id.*

One rationale for the use of MERs for antibiotic drugs is the conflict between the need to restrict access to the drug, to limit antibiotic resistance, and companies' incentive to sell the drug as widely as possible, as often as possible, during the monopoly. James Love & Tim Hubbard, *Prizes for Innovation of New Medicines and Vaccines*, 18 ANNALS HEALTH L. 155 (2009). MERs are seen as

allowing society to conserve the biologic resource, while providing robust incentives to drug developers. *Id.*

C. Government and Charity Funding of Research on New Uses for Approved Drugs

The National Institutes of Health (NIH), other federal agencies, and other non-industry sources fund clinical trials registered at ClinicalTrials.gov, an online database of clinical trial information maintained by the NIH which allows users to search 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. On December 15, 2020, 19,051 trials in the database were classified as interventional studies with completed results, in Phase 2 or 3 (the types of 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.

D. World Intellectual Property Organization Study

The World Intellectual Property Organization (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 the United States has joined. *Patent-related Treaties administered by*

WIPO, https://www.wipo.int/patent-law/en/treaties.html. WIPO has published a study of alternatives to the patent system to support R&D efforts: *Alternatives to the Patent System that are used to Support R&D Efforts*, WIPO, CDIP/14/INF/12 (Sept. 19, 2014), http://www.wipo.int/edocs/mdocs/mdocs/en/cdip_14/cdip_14_inf_12.pdf.

E. Research Mandates

Congress has authorized the FDA to mandate post-approval research on drugs, vaccines and medical devices, and has considered several mandates to fund or undertake research, including on new uses for products, independent evaluation of medical outcomes and other purposes. *See KEI Research Note: 2020-4*, https://www.keionline.org/research-mandates. Research mandates are also used to promote innovation in other sectors, for example, in agriculture for producers of honey, potatoes, soybeans, cotton, etc. *See id.*

CONCLUSION

Courts have been asked to expand patent protection of new uses of older medicines. This task is fraught with challenges, due to the mismatch between the patent system and competing policy objectives of rewarding one invention and not 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. For pharmaceutical drugs, policymakers have options much

broader than patent exclusivity to address such issues. The Panel should grant Teva's petition, understanding that policymakers are best suited to explore how to advance biomedical research without harming competition, affordability and access to older drugs.

Dated: December 28, 2020

Respectfully Submitted,

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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 2317 words, exclusive of the parts exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2).

Dated: December 28, 2020

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