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SUPREME COURT COPY

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IN THE SUPREME COURT OF CALIFORNIA

T.H. AND CARDWELL HAMILTON

Plaintiffs and Appellants,

v.

NOVARTIS PHARMACEUTICALS CORP.,

Defendant and Respondent

Review of a Decision of the Court of Appeal, Fourth Appellate District, Division One, Case No. D067839 (McConnell, P.J.)

From a Decision of the Superior Court San Diego County, Case No. 37-2013-00070440-CU-MM-CTL (Lewis, J.)

APPLICATION BY THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA TO FILE AN *AMICUS CURIAE* BRIEF IN SUPPORT OF NOVARTIS PHARMACEUTICALS CORP.

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December 7, 2016

Attorneys for Amicus Curiae Pharmaceutical Research and Manufacturers of America

Pursuant to Appellate Rule 8.520(f), the Pharmaceutical Research and Manufacturers of America ("PhRMA") respectfully seeks leave to file the accompanying *amicus curiae* brief in support of Defendant Novartis Pharmaceuticals Corp.[1]

PhRMA is a voluntary, nonprofit association comprised of the leading pharmaceutical research and technology companies. PhRMA members are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. In 2015 alone, PhRMA members invested $58.8 billion in discovering and developing new medicines. (PhRMA, *2016 Profile: Biopharmaceutical Research Industry* (2016) p. ii <http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf>.)

PhRMA frequently files amicus briefs on issues that affect its members, and the issue presented in this case is especially crucial to them. Every brand-name company faces generic competition. By expanding the already substantial litigation risks that brand-name companies face to encompass the risks created by their generic competitors' products, the Court of Appeal's outlier holding subjects each of PhRMA's members to unpredictable and potentially immense liability. PhRMA is uniquely positioned to address the unfairness to its members of the Court of Appeal's decision and the accompanying effect that the decision could have on innovation and the public health. PhRMA believes its views will assist the

[1] No party's counsel authored this brief in whole or in part. No party or party's counsel made a monetary contribution intended to fund the preparation or submission of this brief, and no person other than amicus curiae, its members, or its counsel made such a monetary contribution. Although Defendant is a member of PhRMA, it has not contributed financially to the preparation of this brief.

Court in resolving this case by providing a unique perspective on the practical implications of affirming the decision below.

Respectfully submitted,

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Dated: December 7, 2016

PROOF OF SERVICE

I, Romeo Berana, am a resident of the State of California and over the age of 18 years. Neither I, nor my client, the Pharmaceutical Research and Manufacturers of America, are a party to this action. My business address is Covington & Burling LLP, One Front Street, San Francisco, CA 94111.

On December 7, 2016, I caused the following document entitled:

APPLICATION BY THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA TO FILE AN *AMICUS CURIAE* BRIEF IN SUPPORT OF NOVARTIS PHARMACEUTICALS CORP.

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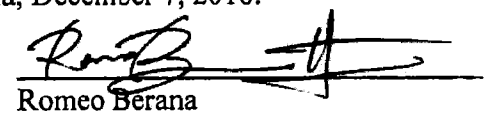
I declare under the penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed in San Francisco, California, December 7, 2016.



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December 7, 2016

CERTIFICATE OF INTERESTED ENTITIES OR PERSONS

Pursuant to Appellate Rule 8.208, the Pharmaceutical Research and Manufacturers of America ("PhRMA") states that it is a trade association with no parent corporations. No entity or person has a 10% or greater ownership interest in PhRMA. PhRMA does not know of any person or entity, other than the parties themselves, that has a financial or other interest in the outcome of the proceeding that the justices should consider in determining whether to disqualify themselves. A list of PhRMA's member companies can be found at http://www.phrma.org/about/member-companies.

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Mannix & Gaba, *Acquiring Pharmaceutical or Medical Device Manufacturers: Due Diligence and Risk Reduction Strategies*, Practical L.J. (Sept. 2012) <https://www.hklaw.com/files/Publication/4649d747-75f5-4165-931c-5d959869a9e3/Presentation/PublicationAttachment/0fb0d029-1301-4442-9fe4-0a9ee7e1fa6d/September2012_MA-in-Healthcare.pdf> 22

National Research Council, Committee on Contraceptive Development, & Institute of Medicine, Division of International Health, *Developing New Contraceptives* (1990) <www.nap.edu/download/1450#> 12

Noah, *Adding Insult to Injury: Paying for Harms Caused by a Competitor's Copycat Product* (2010) 45 Tort Trial & Ins. Prac. L.J. 673 16

Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs* (2003) 54 S.C. L.Rev. 741 ..... 11, 14

Nuangchamnong & Niebyl, *Doxylamine Succinate–Pyridoxine Hydrochloride (Diclegis) for the Management of Nausea and Vomiting in Pregnancy: An Overview* (2014) Int'l J. Women's Health 401 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3990370/pdf/ ijwh-6-401.pdf> 12

PhRMA, *2016 Profile: Biopharmaceutical Research Industry* (2016) <http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf> ..... *Passim*

PhRMA, *Annual Membership Survey* (2015) <http://www.phrma.org/sites/default/files/pdf/2015-phrma_profile_membership_results.pdf> 4

PhRMA, *Biopharmaceutical Research & Development: The Process Behind New Medicines* (2015) <http://www.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf> 2

SUMMARY OF ARGUMENT

Plaintiffs seek to hold Novartis responsible for the alleged injuries of a child whose mother ingested a generic version of its former brand-name medicine Brethine, notwithstanding that Plaintiffs' mother never took the brand-name version of Brethine and that Novartis had stopped marketing Brethine many years earlier. In allowing their claims to proceed, the Court of Appeal embraced several outlier theories that, in addition to being inherently unfair, carry significant public health implications. Faced with uncertain and unlimited liability tethered neither to their own products nor to their financial returns, brand-name companies who face potential liability for alleged injuries sustained while using generic copies of their products years after leaving the market may be forced to cabin that liability in at least two ways that will frustrate the aims of the federal regulatory scheme governing pharmaceuticals and harm public health.

First, by subjecting the companies engaged in innovation to liability that bears no relation to their products or revenues (and that instead follows directly from the measure by which their revenues are reduced by generic competition), the Court of Appeal's holding substantially disrupts innovators' ability to recapture investments and shrinks the resources that can be invested in future innovation.

Second, by creating a remarkable risk profile for brand-name companies, the Court of Appeal's decision encourages companies to prophylactically warn of every conceivable risk, which in turn could erode the meaningfulness of scientifically-justified warnings and deter beneficial uses of medications.

In light of these significant public health concerns, the Court of Appeal's decision should be reversed.

ARGUMENT

I. The Costs of Researching and Developing Innovative Medicines Are Borne Almost Entirely by Brand-Name Companies

A. Innovator Companies Invest Immense Resources in Researching and Developing New Medicines

Bringing a new medicine to market is a lengthy and expensive process. Before studying a new medicine in humans, a pharmaceutical company must conduct a series of laboratory and animal studies to test how the medicine works and assess its safety. (21 C.F.R. § 312.23(a)(8).) If the results are promising, the company submits an Investigational New Drug application ("IND") to the FDA, outlining the preclinical study results and offering a plan for clinical trials in humans. (21 U.S.C. § 355(i)(2); 21 C.F.R. § 312.20(a)–(b).) Upon FDA approval of the IND, the company conducts three phases of clinical trials, each of which must be completed successfully before the potential new medicine may undergo FDA review and approval. (21 C.F.R. § 312.21.) On average, the clinical trial phase takes six to seven years to complete. (PhRMA, *Biopharmaceutical Research & Development: The Process Behind New Medicines* (2015) p. 10 <http://www.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf>.) If clinical trial results show that the medicine's benefits outweigh its risks, the sponsoring company can seek the FDA's approval to market the medicine by submitting a New Drug Application ("NDA"). (21 U.S.C. § 355(b).) The NDA, which must contain, among other things, the results of the clinical and pre-clinical testing, proposals for manufacturing, and proposed labeling for the new medicine (21 U.S.C § 355(b)(1)), often exceeds 100,000 pages in length (PhRMA, *Biopharmaceutical Research & Development*, *supra*, at p. 14).

Innovative companies undertake this process at tremendous expense and risk. On average, developing and obtaining FDA approval of a new medicine takes ten to fifteen years and costs $2.6 billion. (PhRMA, *2016*

Profile: Biopharmaceutical Research Industry (2016) p. ii <http://phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf>.) Pharmaceutical companies spend even more money developing compounds that are never approved: just one out of every 5,000 to 10,000 compounds under development, and just one out of every eight medicines entering clinical trials, obtains FDA approval. (*Ibid.*; PhRMA, *Biopharmaceutical Research & Development*, *supra*, at p. 10; see also PhRMA, *2016 Profile*, *supra*, at p. 36 [reporting that in 2013, pharmaceutical companies sponsored 6,199 clinical trials involving 1.1 million participants].) PhRMA's member companies invest approximately one quarter of their total annual domestic sales on research and development — an estimated $58.8 billion in 2015. (*Ibid.*)

These costs do not end with approval. Once a new medicine is brought to market, NDA holders are required to monitor, review, and report to the FDA all adverse events received from any source, "including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers." (21 C.F.R. § 314.80(b); see also Food & Drug Administration, *Reports Received and Reports Entered into FAERS by Year* (2015) <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070434.htm> [stating that the FDA received over 1.2 million adverse event reports from pharmaceutical companies in 2014].) NDA holders must also submit to the FDA annual reports summarizing all information received about their medicines, including adverse drug events and clinical trial results. (21 C.F.R. § 314.81(b)(2).)

Apart from adverse-event reporting, the FDA frequently requires NDA holders to undertake additional clinical studies after approval. (See

21 U.S.C. § 355(o)(3).) According to one estimate, more than three quarters of all new medicine approvals are accompanied by a commitment by the sponsor to conduct one or more post-marketing, or "Phase IV," studies. (Steenburg, *The Food and Drug Administration's Use of Postmarketing (Phase IV) Study Requirements: Exception to the Rule?* (2006) 61 Food & Drug L.J. 295, 300.) PhRMA's member companies spend more than $7.5 billion annually conducting these studies. (PhRMA, *Annual Membership Survey* (2015) p. 6 table 4 <http://www.phrma.org/sites/default/files/pdf/2015-phrma_profile_membership_results.pdf>.)

B. The Hatch-Waxman Amendments Enable Generic Manufacturers to Copy Innovative Medicines at Minimal Expense

Prior to the passage of the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. No. 98-417 (Sept. 24, 1984) 98 Stat. 1585), commonly known as the Hatch-Waxman Amendments, virtually all companies were required to conduct pre-clinical and clinical trials as a prerequisite to obtaining the FDA's approval to market a medicine. Recognizing that this procedure was a hindrance to the launch of generic medicines — in 1984, approximately 150 medicines with expired patents lacked generic competition — Congress amended the FDA approval process to "make available more low cost generic drugs." (H.R. Rep. No. 98-857, pt. 1, 2d Sess., p. 14 (1984), reprinted in 1984 U.S. Code Cong. & Admin. News, p. 2647.)

The Hatch-Waxman Amendments left in place the multi-step approval process for innovative new medicines, but it streamlined that process for generic versions of those medicines. Under Hatch-Waxman, a company may seek approval to market a generic medicine by filing an abbreviated new drug application ("ANDA") demonstrating that the generic version is biologically equivalent to an already-approved medicine. (21

U.S.C. § 355(j)(2)(A)(iv); 21 C.F.R. § 314.92(a)(1).) An ANDA applicant need not independently perform extensive and costly studies to prove that the generic is safe and effective; instead, it can rely on "a prior agency finding of safety and effectiveness based on the evidence presented in [the] previously approved new drug application." (57 Fed. Reg. 17950, 17953 (April 28, 1992).)[1]

Due to these streamlined procedures, researching and developing a generic version of an FDA-approved medicine costs under $2 million today — less than one-tenth of one percent of the cost of developing the innovative medicine itself. (U.S. Department of Health and Human Services, Office of Science and Data Policy, *Expanding Use of Generic Drugs* (2010) pp. 4–5 <https://aspe.hhs.gov/sites/default/files/pdf/76151/ib.pdf>.) Generic manufacturers pass these cost savings onto consumers. (See PhRMA, *Biopharmaceuticals in Perspective: Spring 2016* (2016) p. 54 <http://phrma.org/files/dmfile/chart-pack-biopharmaceuticals-in-perspective4.pdf>.)

II. The Duties Created by the Court of Appeal Would Expose Brand-Name Companies to Limitless Liability

Plaintiffs take great pains to portray this case as unique. In truth, there is nothing particularly unusual about the allegations presented here. After generic entry, the market share of generic copies of medicines dwarfs the brand's market share. (See, e.g., Grabowski, *Updated Trends in US Brand-Name and Generic Drug Competition* (2016) 19 J. Med. Econ. 836 [reporting that for brand medicines facing generic entry in 2013-2014, generics captured an average of 93 percent of the market (by volume)

[1] Because a generic medicine must contain "the same" active ingredient(s), delivered in "the same" dosage form, strength, and route of administration, in a formulation that is bioequivalent to an approved brand-name medicine, it must bear identical warnings. (28 U.S.C. § 355(j)(2)(A)(ii)–(v).)

within the first year].) If allowed to stand, the Court of Appeal's decision will expose brand-name manufacturers to virtually unlimited liability for injuries allegedly sustained while using generic versions of their current and former branded products.

The scope of litigation against pharmaceutical companies is immense. Between 2000 and 2006, more than 65,000 product liability lawsuits were filed against pharmaceutical companies. (See Schmit, *More Drugs Get Slapped with Lawsuits* (Aug. 23, 2006) USA Today <http://usatoday30.usatoday.com/money/industries/health/drugs/2006-08-23-drug-lawsuits-usat_x.htm>.) And as of last year, one quarter of all pending multidistrict litigation proceedings involved product liability claims, the majority involving medicines or medical devices. (See U.S. Judicial Panel on Multidistrict Litigation, Calendar Year Statistics: January Through December 2015, p. 11 <http://www.jpml.uscourts.gov/sites/jpml/files/JPML_Calendar_Year_Statistics-2015.pdf>.)

Lawsuits seeking to impose innovator liability on brand-name pharmaceutical companies already number in the thousands. (See *Neeley v. Wolters Kluwer Health, Inc.* (E.D. Ky. 2015) 311 F.R.D. 427, 429 [noting that "thousands" of cases have been filed against "against various generic and brand-name companies responsible for manufacturing Reglan®/metoclopramide"].) Courts have ruled on this issue in lawsuits involving treatments for allergic reactions, asthma, bacterial infections, cardiac arrhythmias, depression, enlarged prostate, heartburn, insomnia, menopausal symptoms, migraine headaches, obesity, and panic disorder, to name just a few.[2] Cases seeking to hold brand-name companies liable

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[2] See, e.g., *Foster v. American Home Products Corp.* (4th Cir. 1994) 29 F.3d 165, 168–71 [Phenergan (promethazine hydrochloride)]; *Tsavaris v. Pfizer, Inc.* (S.D. Fla. 2016) 154 F.Supp.3d 1327, 1339–41 [Activella (continued...)

under a theory of innovator liability persist, even though the concept has been rejected by the overwhelming majority of courts that have considered it. (See Opening Brief on the Merits pp. 32–33.)

Should innovator liability gain acceptance, the number of lawsuits would multiply exponentially. A creative advocate can always sketch out a scenario where some action (or inaction) by the brand-name company years earlier could impact the subsequent generic labeling. There is virtually no limiting principle to this "butterfly effect" rational endorsed by the Court of Appeal, as clever lawyers can trace almost any safety issue back to the original brand holder, given the overwhelming amount of safety data the innovator company amasses over the decades of development and marketing of a medicine before generic entry. Lawyers can almost always make incendiary allegations of "off-label" promotion for unapproved uses, to conceive of new or stronger warnings that they allege companies should have added to their labeling, or to claim in hindsight that existing warnings should have been added sooner. (See, e.g., Brief for the United States as

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(estradiol/norethindrone acetate)]; *Neeley v. Wolters Kluwer Health, Inc.*, *supra*, 311 F.R.D. 427, 432–34 [Reglan (metoclopramide)]; *Anselmo v. Sanofi-Aventis Inc. USA* (Kan. Dist. Ct., Oct. 13, 2014, No. 10-CV-77) 2014 WL 8849464, at *1 [Ambien (zolpidem)]; *Barnhill v. Teva Pharmaceuticals USA, Inc.* (S.D. Ala., Apr. 24, 2007, No. CIV A 06-0282-CB-M) 2007 WL 5787186, at *2 [Keflex (cephalexin)]; *Goldych v. Eli Lilly & Co.* (N.D.N.Y., July 19, 2006, No. 5:04CV1477(GLS/GJD)) 2006 WL 2038436, at *3–8 [Prozac (fluoxetine)]; *Colacicco v. Apotex, Inc.* (E.D. Pa. 2006) 432 F.Supp.2d 514, 539–43 [Paxil (paroxetine)]; *DaCosta v. Novartis AG* (D. Or., Mar. 1, 2002, No. CV 01-800-BR) 2002 WL 31957424, at *8–9 [Migranal (ergot alkaloid)]; *Rafferty v. Merck & Co., Inc.* (Mass. Super., May 23, 2016, No. 2013–04459) 2016 WL 3064255, at *4–6 [Proscar (finasteride)]; *Stanley v. Wyeth, Inc.* (La. Ct. App. 2008) 991 So.2d 31, 33–35 [Cordarone (amiodarone)]; *Flynn v. American Home Products Corp.* (Minn. Ct. App. 2001) 627 N.W.2d 342, 350–52 [Pondimin (fenfluramine)].

Amicus Curiae Supporting Petitioner p. 25, *Wyeth v. Levine* (2009) 555 U.S. 555 (No. 06-1249) <http://www.americanbar.org/content/dam/aba/publishing/preview/publiced_preview_briefs_pdfs_07_08_06_1249_PetitionerAmCuUSA.authcheckdam.pdf> [noting the "post hoc imagination of lawyers" in pursuing pharmaceutical lawsuits challenging safety labeling].) And because nine out of every ten U.S. prescriptions are filled with generics, the number of potential plaintiffs is enormous. (PhRMA, *2016 Profile*, *supra*, at p. ii).

As this case demonstrates, a broad interpretation of such allegations can permit even the most outlandish claims to survive demurrer, forcing companies to expend significant resources and years in discovery to fend off frivolous claims. For example, Plaintiffs claim that Novartis failed to warn of the "serious side effects on newborns whose mothers consumed Terbutaline while pregnant" (AA016–58, at ¶ 130), notwithstanding that more than three years after T.H.'s mother ingested terbutaline, the FDA concluded that "the available human data regarding an association between terbutaline sulfate and autism" — the specific disorder from which T.H. allegedly suffers — "are not sufficient to conclude that there is 'positive evidence of human fetal risk.'" (Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, to James P. Reichmann (Feb. 17, 2011) p. 13 <http://www.fda.gov/downloads/drugs/drugsafety/ucm243797.pdf>.) Plaintiffs further complain that Novartis "aggressively marketed" Brethine for an off-label use (Answer Brief on the Merits p. 12), notwithstanding that the FDA has never challenged Novartis's marketing of Brethine.[3]

[3] While Plaintiffs contend that off-label promotion "goes dramatically under-regulated by the FDA" (Answer Brief on the Merits p. 40), the truth of the matter is that the federal government and state attorneys general (continued...)