No. _____

# In The
# Supreme Court of the United States

WENDY B. DOLIN, Individually and as Independent Executor of the Estate of STEWART DOLIN, Deceased,

*Petitioner,*

v.

GLAXOSMITHKLINE, LLC, Formerly Known as SMITHKLINE BEECHAM CORPORATION,

*Respondent.*

**On Petition For Writ Of Certiorari To The United States Court Of Appeals For The Seventh Circuit**

## PETITION FOR WRIT OF CERTIORARI

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## QUESTION PRESENTED

In *Wyeth v. Levine*, 555 U.S. 555 (2009), this Court held "impossibility pre-emption is a demanding defense" and, "absent clear evidence that the FDA would not have approved a change to [a drug's] label, we will not conclude that it was impossible for [drug manufacturer] to comply with both federal and state requirements." *Id*. at 571, 573.

In this case, the Seventh Circuit vacated a jury's verdict and found that, notwithstanding the fact "[the drug manufacturer] re-analyzed the placebo-controlled data on [its drug] and found a link between [its drug] and suicide in adults" (App. 23), the manufacturer was not permitted to issue a warning because FDA had implemented a class-wide suicide warning for such drugs which did not extend to adult patients beyond age 24. *Id*. The court found preemption even though an FDA expert testified the manufacturer was permitted to add its drug-specific suicide warning and the FDA had advised the manufacturer to submit its drug-specific warning using a procedure that allows manufacturers to strengthen warnings. App. 47-55.

In vacating the jury's verdict, the Seventh Circuit opined "no reasonable jury could find that the FDA would have approved an adult-suicidality warning . . . " (App. 22). The court failed to appreciate the heightened evidence required under *Levine*, and failed to review the evidence in a light most favorable to the plaintiff.

The question presented is: Does federal law prevent a drug manufacturer from enhancing its label to

**QUESTION PRESENTED** – Continued

reflect truthful risks revealed in its clinical trials when the relevant FDA regulations allow a manufacturer to make unilateral labeling changes and when the FDA encouraged the manufacturer to utilize those regulations to submit an appropriate labeling change?

## PARTIES TO THE PROCEEDING

Petitioner, Wendy B. Dolin, was the plaintiff in the district court and appellee in the court of appeal. She initiated the underlying wrongful death lawsuit in her individual capacity and as executor of the estate of her deceased husband, Stewart Dolin.

Respondent, GlaxoSmithKline, LLC, formerly known as SmithKline Beecham Corporation, was the defendant in the district court and appellant in the court of appeals.

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## INTRODUCTION

This case raises an issue of recurring importance (federal preemption of common law pharmaceutical products liability claims) in which the decision of the Seventh Circuit directly conflicts with that of the Third Circuit, and more importantly, is at odds with this Court's seminal decision in *Wyeth v. Levine*, 555 U.S. 555 (2009). This Court now has before it the conflicting Third Circuit case, *Merck v. Albrecht*, Case No. 17-290. In the present case, the Seventh Circuit erroneously held that petitioner's claims for failure to provide adequate warnings against the brand-name manufacturer and author of the warnings were preempted because "federal law prevented [the brand-name manufacturer] from adding a warning" about a risk associated with the drug. App. 4. Factually, the present case is very similar to *Albrecht*. Because the Court's resolution of *Albrecht* is likely to provide needed guidance to the courts below on how to assess a preemption defense in this context, the petition should be held pending the Court's disposition of *Albrecht*, and then the Seventh Circuit's ruling vacated and remanded for further proceedings in the Seventh Circuit.

Independent of the Court's resolution in *Albrecht*, the petition here should be granted because this case raises important questions that are not likely to be resolved in *Albrecht*. In this case, unlike *Albrecht*, the Food and Drug Administration ("FDA") requested that a class-wide suicide warning be implemented for all antidepressants on the market based on a pooled

meta-analysis of a number of different antidepressants, but not all of them.

The question remains, however, does the FDA's implementation of a class warning prohibit a manufacturer from issuing additional warnings if the manufacturer's own clinical trial data and analysis reveal that its drug poses a greater risk than that expressed in the class-label? Every district court to analyze this issue, other than the Seventh Circuit in this case, has held the manufacturer remained free to utilize the Changes Being Effected provision (App. 69-70) of the Food Drug and Cosmetic Act ("FDCA") to unilaterally add warnings unique to its drug.

Furthermore, unlike *Albrecht*, the facts here are even more compelling. The FDA specifically told the manufacturer that, if it wanted to enhance the label concerning the Paxil-specific suicide risks, it should either submit a supplement as it statutorily was permitted to do, or request a formal meeting to discuss the matter further. App. 100 & 113-114. GSK did neither. Nonetheless, the Seventh Circuit ruled there was clear evidence the FDA would have rejected an adult-suicidality warning. App. 24-26.

Finally, the relevant events and duties in this case arose prior to revisions of the regulations governing unilateral labeling changes by drug manufacturers. *See* 21 C.F.R. § 314.70(c)(2)(i) (May 23, 1985-June 29, 2006) (App. 69) & 21 C.F.R. § 314.70(c)(6)(iii)(A) (June 30, 2006-September 21, 2008) (App. 117) vs. 21 C.F.R. § 314.70(c)(6)(iii) (September 22, 2008-Present) (App.

118). The Seventh Circuit, however, adjudicated the case utilizing the subsequently enacted (post 2008) regulations as opposed to the regulations in effect at the time the duties arose. Thus, there is also an issue of whether the Seventh Circuit impermissibly retroactively applied key regulations resulting in defendant being absolved of its duties and responsibilities under the prior applicable regulations. This petition presents questions that are significant in their own right, and the Court should grant the petition irrespective of its handling in *Albrecht*.

## OPINIONS BELOW

The district court's opinion denying defendant-respondent's motion for summary judgment (App. 62-66) appears at 2016 WL 537949. The district court's order denying defendant-respondent's motions for judgment as a matter of law or for a new trial (App. 30-61) was reported at 269 F.Supp. 3d 851. The Seventh Circuit's decision reversing the jury's verdict and the judgment of the district court (App. 1-29) was reported at 901 F.3d 803.

## JURISDICTION

The Seventh Circuit entered its judgment on August 22, 2018, *see* App. 1, and denied petitioner's timely petition for rehearing and rehearing *en banc* on

September 20, 2018, *see* App. 67-68. This Court has jurisdiction under 28 U.S.C. § 1254(1).

## PROVISIONS INVOLVED

Relevant statutory and regulatory provisions are reproduced at App. 69-74, 117-119.

## STATEMENT OF THE CASE

### A. Regulatory Background

The history of the FDCA, as well as its predecessors, demonstrate that Congress' primary motivation for enacting the statute was to protect the health and safety of the public. *Wyeth v. Levine*, 555 U.S. 555, 567, 579 (2009). When a series of deadly reactions to a diphtheria vaccine in 1902 killed numerous children in Camden, New Jersey, Congress combined the concerns about adulterated foods and unsafe drugs to pass the Biologics Controls Act of 1902, ch. 1378, 32 Stat. 728 (1902); *see also* STEPHEN J. CECCOLI, PILL POLITICS: DRUGS AND THE FDA 62 (2004). Congress followed with the Pure Food and Drugs Act of 1906, which prohibited the manufacture of any drug that was "adulterated or misbranded." *See* Pure Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768 (1906).

Then, most relevant to the present case, in 1938, when reports revealed the "miracle" drug Elixir Sulfanilamide had caused hundreds of individuals to be

poisoned and had killed over 100 people, including children, Congress enacted the Food, Drug, and Cosmetic Act of 1938, ch. 675, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301 et seq.); *see also* CECCOLI at 70-71. The Act required that drug manufacturers provide proof their products were *safe* before they could be marketed. Subsequently, the thalidomide incident (a sleeping pill that caused severe birth defects worldwide) in the early 1960s led to the passage of the Kefauver-Harris Amendments to the FDCA, which required that drugs be proven to be safe and effective before release. *See* Drug Amendments of 1962, Pub. L. No. 87-781, § 102, 76 Stat. 780, 781 (1962) (codified as amended at 21 U.S.C. § 355); *see also* CECCOLI at 76-79. It is thus evident that, from its inception, the FDCA and similar Acts of Congress were enacted to protect the health and safety of the public against sometimes indiscriminate pharmaceutical manufacturers.

Importantly, as this Court has already recognized, the predecessor statutes to the FDCA, the FDCA and its subsequent amendments were all passed amidst a background history of state-law tort lawsuits against drug manufacturers, including failure-to-warn claims for dangerous side effects. *Levine*, 555 U.S. at 567 ("As it enlarged the FDA's powers to 'protect the public health' and 'assure the safety, effectiveness, and reliability of drugs,'. . . . Congress took care to preserve state law.") Congress declined to insert a federal cause of action in the FDCA, determining that "widely available state rights of action provided appropriate relief for injured consumers." *Levine*, 555 U.S. at 574.

The FDCA generally forbids the sale of a prescription drug in interstate commerce unless it has been approved by the FDA. 21 U.S.C. § 355(a). A manufacturer seeking approval of a brand-name drug must file a new drug application ("NDA") with FDA. An NDA includes proposed labeling. *Id.* § 355(b)(1)(F).

Nothing in the FDCA prohibits a manufacturer from changing the label of a brand-name drug after FDA approval, so long as the label does not render the drug "misbranded." *See id.* §§ 331(a), 352(a) (drug is misbranded "[i]f its labeling is false or misleading in any particular"). Changing an approved label does not, on its own, render a drug misbranded, and this Court has found it "difficult to accept" that "FDA would bring an enforcement action against a manufacturer for strengthening a warning." *Levine*, 555 U.S. at 570.

FDA regulations long have expressly authorized brand-name drug manufacturers to revise labeling unilaterally to strengthen warning language. FDA first promulgated such a regulation in 1965. *See* 30 Fed.Reg. 993, 993-94 (1965); 21 C.F.R. § 130.9(d)(1), (e) (1966). While undergoing various numbering revisions and verbiage changes, throughout the period relevant to this case (1990s through 2010), the regulations continued to permit manufacturers to utilize what is known as the "Changes Being Effected" ("CBE") provision unilaterally to enhance the warnings in their drug label *without* advance approval from the FDA. *See*, *e.g.*, 50 Fed.Reg. 7452-01, 7499 (1985); 21 C.F.R. § 314.70(c)(2)(i) (May 23, 1985-June 29, 2006) (App. 69-70); 21 C.F.R. § 314.70(c)(6)(iii)(A) (June 30,

2006-Present) (App. 117). Importantly, prior to September 22, 2008, the regulations gave broad authority to the manufacturer to enhance its warnings, at any time and as it saw fit, "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction." *See* 21 C.F.R. § 314.70(c)(2)(i) (May 23, 1985-June 29, 2006) (App. 69-70); 21 C.F.R. § 314.70(c)(6)(iii)(A) (June 30, 2006-September 21, 2008) (App. 117). On September 22, 2008, the CBE regulation was substantively revised in two relevant ways. First, beginning in September 2008, the regulations now require that labeling be revised by manufacturers when they possess "*newly acquired information*" of a risk.[1] 21 C.F.R. § 314.70(c)(6)(iii) (September 22, 2008-Present) (App. 118). Second, the regulations now require there be evidence of a *causal association* between the drug and the risk. 21 C.F.R. § 314.70(c)(6)(iii)(A) (App. 118).

FDA regulations also establish the format of drug labeling. Relevant to the present case, in 2006, the regulations governing drug labeling were substantively revised, however, for "older drugs" (i.e., generally, drugs approved prior to 2001 (five years prior to the effective date of the revisions)), the labeling regulations continued to be governed by the older rules, which were renumbered and re-codified in 21 C.F.R. § 201.80(e), while the regulations governing "new" drugs are located at 21 C.F.R. § 201.57(c). It is undisputed that

[1] "Newly acquired information" includes "data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses)." 21 C.F.R. § 314.3(b).

Paxil (paroxetine), the drug at issue in this case, which was approved in 1992, is an "older" drug and thus its labeling is governed by 21 C.F.R. § 201.80(e) (which essentially contains the language of the pre-2006 version of 21 § 201.57(e)) (*see* App. 71-72). For purposes of this case, and with respect to the question of a manufacturer's duty to revise its label, both the regulations governing older drugs and the regulations governing new drugs provide that the labeling "*shall*" (or "must") be revised as soon as there is evidence of an association of a serious hazard with a drug. *See* 21 C.F.R. § 201.80(e) (old drugs) (App. 71); cf. 21 C.F.R. § 201.57(c) (new drugs).

Until the Food and Drug Administration Amendments Act of 2007 ("FDAAA") (September 27, 2007), FDA lacked authority to mandate that manufacturers change prescription drug labels. *See Levine*, 555 U.S. at 571. The FDAAA gave FDA authority to initiate a process to mandate label changes if FDA "becomes aware of new safety information" that FDA "believes should be included in the labeling of the drug." 21 U.S.C. § 355(o)(4)(A). Congress included a "[r]ule of construction" that "[t]his paragraph shall not be construed to affect the responsibility of the [manufacturer] to maintain its label in accordance with existing requirements, including . . . [21 C.F.R. §] 314.70." *Id*. § 355(o)(4)(I).

### B. Paxil (Paroxetine) and Its Label

Paroxetine is a psychotropic drug in a class of drugs called Selective Serotonin Reuptake Inhibitors ("SSRI"), marketed under the brand name Paxil. App. 3. The FDA approved it in 1992. App. 9.

From GSK's initial clinical trials, GSK had data demonstrating paroxetine increases the risk of adult suicidal behavior, i.e., suicides and suicide attempts. App. 45-46. Paroxetine induces suicidal behavior through a combination of akathisia, emotional blunting, and decompensation. *See* R.617, Tr.*207:12-215:25; R.618; *223:8-224:7, *227:6-228:14, *233:4-244:25.

Akathisia is a psychological (inner) and physiological (outer) phenomenon, induced by drugs like paroxetine. "People have described it like a state worse than death. . . ." R.617, Tr.*209:9-13. Emotional blunting is psychological numbing, where a person loses the ability to consider the consequences of their actions. R.618, Tr.*233:4-235:11. Decompensation refers to a psychotic break. R.618, Tr.*238:15-239:12. There is scientific consensus that these phenomena, akathisia in particular, can lead to suicide. R.635, Tr.*2300:25-2302:18; R.651, Tr.*4136:17-19; App. 48-49.

When *properly* analyzed, GSK's original paroxetine studies revealed that adult patients of all ages given paroxetine, as opposed to placebo, were nearly nine-times more likely to either attempt suicide or successfully kill themselves. R.629 at 96-97 (R.629, *Tr. 963-964). These results were statistically significant (p-value of .04). *Id*. GSK, however, concealed this risk

by improperly reporting the study results. Specifically, GSK inflated the number of suicide and suicide attempts in the placebo group by improperly counting events that occurred in the "run-in" period—the period where all patients are given placebo pills to wash out other drugs in their system *before* entering the study. App. 45-46; *see also* R.619, Tr.*362:21-365:9. Counting events during the run-in period is scientifically "illegitimate." R.555-1 at *210:11-22; R.629, Tr.*956:18-23. Increasing the number of events in the placebo group hid the elevated rates in the paroxetine portion. R.619, Tr.*474:8-476:8; R.620, Tr.*505:6-20; R.629, Tr.*956:24-957:17; R.630, Tr.*996:9-997:3. When the events are properly counted, the data shows, among already-depressed patients, a statistically-significant *8.9-fold* increase in the risk of suicidal behavior when taking paroxetine. R.629, Tr.*963:20-964:7; R.630, *996:9-997:3; *see also* App. 45-46.

In 1992, the FDA approved paroxetine and GSK's proposed labeling did not warn about a suicide risk with paroxetine. R.668-12 at 1-2; R.630, Tr.*994:1-21, *995:4-998:11. Rather, the label stated that "[t]he possibility of a suicide attempt is inherent in depression[.]" R.668-12 at 2. This "precaution" only linked the suicide risk to the underlying disease (depression) and did not warn that paroxetine (the drug) itself could increase the risk of suicide.

In 1999, a GSK researcher not involved in the original data tabulation, noticed GSK was improperly counting run-in suicides and that the data, when analyzed properly, showed that paroxetine is associated

with a suicide risk. R.668-29 at 1. This prompted a GSK executive to concede that the data "seems to be . . . suggesting that Paxil is associated with a higher rate of suicide vs. placebo." R.668-20 at 1. The next day, a GSK regulatory official reached out to the FDA and asked, "hypothetically" whether it would be appropriate to count suicides during the run-in period. R.668-21 at 1-2. The FDA "clearly stated that such a patient should not be counted in our analysis[.]" *Id.* Notwithstanding this response, GSK chose not to take any steps to update its analysis or labeling.

In June 2001, a federal jury returned a $6 million verdict against GSK, finding that GSK's paroxetine label was inadequate with respect to the suicide and violence risks associated with paroxetine. *Estates of Tobin by Tobin v. SmithKline Beecham Pharm.*, 164 F.Supp. 2d 1278, 1280-1288 (D. Wyo. 2001). Notwithstanding the *Tobin* court's ruling and the jury's findings, GSK did not undertake any effort to revise the paroxetine label to warn about suicide risks.

In April 2002, GSK submitted an application seeking FDA approval for pediatric use of paroxetine. *Knipe v. SmithKline Beecham*, 583 F.Supp. 2d 553, 562 (E.D. Pa. 2008). This application was never approved by the FDA because the data failed to show paroxetine is effective in children. *Id*. GSK's application, however, raised red flags concerning GSK's miscoding of suicidality adverse events as "emotional lability." R.668-7; *see also* R.641, Tr.*2969:16-21 (GSK expert defined emotional lability as "variation in mood" and "it's not trying to kill yourself.") When the FDA requested more

information from GSK concerning the "emotional lability" adverse events, it learned that nearly all of the "emotional lability" events were suicide-related. R.668-7 at 1-2. This led the FDA to review the data from other manufacturers to see if they too were hiding suicide events "by various inappropriate coding maneuvers." R.668-7 at 1-2; *see also* R.589-14 at 6-7. In 2004, the FDA reviewed the pediatric data for all SSRIs and concluded, on a class-wide basis, that SSRIs can cause pediatric suicidality. R.589-14 at 7. GSK's submission for pediatric use of Paxil and the eventual discovery of the inappropriate coding maneuvers and suicide risks "was the catalyst for a series of events culminating in the FDA required 'black box' warning" for pediatric suicidality in 2004 which was the first class warning for antidepressants. *Knipe*, 583 F.Supp. 2d at 580.

The FDA then decided to conduct a similar analysis of the adult data for all antidepressants. R.589-14 at 7. The FDA requested placebo-controlled data from all antidepressant NDA holders related to adult suicidality. *Id.* GSK submitted its data in March 2006. R.589-20 at 1-3. However, GSK only submitted data in its central database; it did not include placebo-controlled suicide data from locally-funded paroxetine trials. R.645, Tr.*3361:18-3362:24, *3366:22-3367:9. Indeed, a GSK physician noted that "GSK have data from additional studies, locally run, that are not on our central database but meet the FDA's criteria for studies that qualify for the suicidality analysis." R.645. Tr.*3354:1-3366:17. However, GSK never collected the data from the locally-funded studies and never

submitted it to the FDA. R.645, Tr.*3361:18-3362:24, *3366:22-3367:9. This omission was not inconsequential. In GSK's 2006 submission, it reported *one* suicide in patients taking paroxetine. R.646, Tr.*3512:5-21. But, GSK was aware of multiple suicides in placebo-controlled, locally-funded, clinical trials. R.645, Tr.*3362:8-21; R.646 Tr.*3510:21-24, *3511:21-3512:25.

While GSK's *incomplete* adult suicidality data was being reviewed by the FDA, GSK conducted its own analysis of the data and concluded that paroxetine was associated with a statistically-significant 6.7-fold increased risk of suicidal behavior in depressed adults of all ages. R.589-20 at 2; R.589-21 at 4; *see also* App. 11, 45. Thereafter, in April 2006, GSK unilaterally revised the paroxetine label concerning the risk of suicidality associated with paroxetine in adult patients, as it was permitted to do using the CBE (21 C.F.R. § 314.70). R.589-21 at 1; R.589-22 at 2; *see also* App. 11-12 & 52-53 (quoting from R.589-5 at 11) (containing GSK's added 2006 paroxetine suicide warning).

In December of 2006, several months after GSK unilaterally changed the label, the FDA issued the results of its adult suicidality analysis of 18 different antidepressants, using, in part, *the incomplete data* submitted by GSK. R.589-14 at 7. The pooled analysis of all the drugs combined did not show an elevated risk for suicidality in adults over age 24 for the analyzed antidepressants. *Id.*; *see also* R.591-18. However, the paroxetine-specific data reviewed by the FDA (which was less than the data GSK internally possessed and analyzed), showed a statistically significant 2.76-times

elevated risk for suicidal behavior for paroxetine patients compared to placebo. R.589-14 at 18; App. 13, 45; R.619, *Tr. 449-458 (expert testimony concerning the results and multiple comparisons).

The FDA subsequently requested that manufacturers of all antidepressants on the market (even those not included in the FDA's analysis) add a class-wide warning concerning a suicide risk in children, adolescents, and young adults (under age 24), but indicating that the risk from the FDA's pooled analysis did not show that it extended beyond the age of 24. R.623, Tr.*1126:16-1137:25; R.589-1 at 1-44. While this language may be accurate for the analyzed antidepressants generally, it is not accurate for paroxetine specifically. *Id.*; *see* R.668-15 at 1-44; R.623, Tr.*1138:1-1223:23.

On May 1, 2007, the FDA sent a letter to GSK referencing GSK's previous April 2006 CBE supplement and stated that GSK's enhanced suicide warnings were "approvable" but further asked GSK to add the newly drafted FDA class warning concerning suicide risks:

> **We have completed our review of your supplemental applications, and they are approvable.** Before these applications may be approved, you will need to make revisions to your labeling, as outlined below, so as to ensure standardized labeling pertaining to adult suicidality with all of the drugs to treat major depressive disorder (MDD).

App. 85, emphasis added (R.589-23). This caused some confusion within GSK, as to whether GSK was permitted to include the paroxetine-specific language within the FDA's class labeling. In a May 11, 2007 e-mail, followed up with a May 23, 2007 letter, GSK proposed to include its paroxetine-specific warning *in the middle* of the class-warning. R.589-27, 32.

On June 21, 2007, a project manager for the FDA (Renmeet "Rimmy" Grewal) responded by email stating:

> We also have noted that some sponsors [drug manufacturers] have taken this opportunity to include other revisions to their labeling which are not applicable to the class labeling revision requested in our 5-1-07 letter. **We are requesting that these changes be submitted as a *separate supplement*.**

App. 100, emphasis added (R.589-29). GSK's proposed April 2006 adult suicide warning was not rejected by the FDA, rather the FDA simply asked that GSK issue a separate supplement [CBE]. GSK clearly understood this as reflected in the following internal GSK memorandum discussing the FDA's June 21st communication:

> On June 21, 2007 FDA responded to our CBE submission for [Paxil] (submitted on May 23, 2007). . . . **GSK's request of maintaining the Paxil specific language within the class labeling was not addressed. FDA requested that those additions or**

> **changes should be addressed with a separate supplement.**

App. 113-114, emphasis added. The following day, in response to a GSK voicemail, Rimmy (from FDA) e-mailed GSK stating:

> [T]he Agency has reviewed your proposed changes, and **we do not believe that your product specific analysis should be included in the *class labeling* revisions** since the labeling is targeted at the class of drugs. **If you would like to discuss this matter further, please submit a formal meeting request.**

App. 115, emphasis added (R.589-30). GSK never took the meeting and never proposed revising the label to include any paroxetine-specific warning in any other portion of the label or to correct other inaccuracies in the label (e.g., the label continued to include "emotional lability" as a frequent event without disclosing that most if not all were suicide related). App. 14 & 52-55; *see also* R.623, Tr.*1206:18-1212; R.645, Tr.*3374:6-3376:10, *3375:25-3376:4, *3379:1-20; R.646, Tr.*3510:25-3511:13; and R.645 Tr.*3446:4-3461:12 (GSK testimony regarding company's continuous use of emotional lability to describe suicide events in the label). Instead, the label contained no warning of paroxetine's older adult suicide risks.

The only FDA expert to testify at trial, David Ross, M.D., Ph.D., a former FDA deputy director for regulatory science, senior medical reviewer, and medical officer at the FDA, testified at length regarding the

various places within the overall label (but outside the class-wide portion of the label) GSK could have included a paroxetine-specific adult suicide warning, using the CBE regulations. R.623, Tr.*1147:25-1181:8, *1148:23-1149:9, *1186:5-1211:2, *1212:14-1217:17, *1213:13-17; R.626, *1549:4-7; R.668-16. Dr. Ross also testified about other inadequacies dating back to 1992, and even in GSK's 2006 label. *See*, *e.g.*, R.630, Tr.*1072, *1075-1086; R.623, *1206-1212, *1197-1200, *1166-1167, *1192-1193, *1176. Dr. Ross, relying upon his review of the relevant evidence and his FDA experience (which included reviewing new drug applications, clinical trials, the adequacy of drug labels and making labeling recommendations), testified that "the FDA would not have refused to permit GSK to warn about the risk of adult suicide in the label." App. 47 & 52-55. Moreover, GSK's vice-president and designated company witness, John Kraus, M.D., admitted at trial that the FDA never told GSK it was "prohibited from putting any Paxil-specific information anywhere in the label." R.645, Tr.*3375:16-19.

### C. Case Specific Facts and Procedural History

Stewart Dolin was a loving father, devoted husband and senior partner at Reed Smith, LLP in Chicago. He was experiencing work-related anxiety in June 2010 (R.628, Tr.*1796:8-12) when his doctor, Martin Sachman, M.D., prescribed him Paxil. App. 3. Mr. Dolin's druggist, however, filled his prescription with generic paroxetine, manufactured by Mylan, Inc. App. 32; R.627, Tr.*1668:16-25, *1711:23-1712:4.

At trial, Dr. Sachman testified that he relied on the 2010 paroxetine label in deciding to prescribe paroxetine to Mr. Dolin in 2010; that the 2010 label did not warn that paroxetine could induce suicidal behavior in adults over age 24; that the 2010 label indicated the risk did not extend beyond age 24; he relied on that representation; and, had GSK warned of the risk of adult suicidal behavior over age 24, he would not have prescribed paroxetine to Mr. Dolin. App. 43.

On July 15, 2010 (six days after starting paroxetine), Mr. Dolin left his office, proceeded to a Chicago "L" train. A nurse witnessed Mr. Dolin on the train platform appearing agitated and extremely anxious, nervously pacing around the platform—consistent with drug-induced akathisia—like a caged "polar bear." R.555-5 at *40:7-50:12, *74:7-10; *see also* App. 50. When the O'Hare-bound train pulled into the station, Mr. Dolin jumped in front of the train. *Id.* *51:21-52:6. An autopsy confirmed paroxetine was in his blood. App. 48.

The case was initiated in the Circuit Court of Cook County, Illinois and removed to the Northern District Court of Illinois based on diversity citizenship. App. 31; 28 U.S.C. §§ 1332 & 1441. Following removal, the defendants included GlaxoSmithKline ("GSK") and Mylan, Inc. ("Mylan"). Mylan was the manufacturer of the generic form of paroxetine Mr. Dolin was taking at the time of his suicide. GSK was the brand-name manufacturer and author of the deficient warning label that accompanied generic paroxetine. Relying upon this Court's decisions in *Mut. Pharm. Co., Inc. v. Bartlett*, 570 U.S. 472 (2013) and *PLIVA v. Mensing*, 564 U.S. 604 (2011), the district court dismissed all claims against Mylan on the grounds that plaintiff's claims were preempted because Mylan as a generic manufacturer was prohibited from unilaterally making any changes to the drug label. *Dolin v. SmithKline Beecham Corp*., 62 F.Supp. 3d 705, 723 (N.D. Ill. 2014). The dismissal of Mylan was not challenged on appeal and is not the subject of this petition. Within the same order, the district court held that, under Illinois law, GSK as the brand-name manufacturer bore exclusive responsibility for the paroxetine label and thus owed a duty of care to Mr. Dolin even though Mr. Dolin ingested a generic version of paroxetine. *Dolin*, 62 F.Supp. 3d at 714.[2] While GSK did appeal the district

[2] The Supreme Courts in at least two other states have similarly recognized that, under their common law, a plaintiff injured by a generic drug may maintain common law claims against the brand-name manufacturer if the drug's deficient warning was the cause of the plaintiff's injuries. *T.H. v. Novartis Pharm. Corp*., 4 Cal. 5th 145, 165 (2017) (California) and *Rafferty v. Merck & Co*.,

court's decision on brand-name liability under Illinois law, the Seventh Circuit never addressed this argument and it is not the subject of this petition.

Subsequent to the district court's ruling that GSK owed a duty under Illinois common law, GSK next moved for summary judgment arguing that Mrs. Dolin's claims were preempted by federal law because, according to GSK, the FDA had considered and rejected an adult suicide warning for paroxetine. App. 63-64. The district court noted that "GSK's argument for 'implied conflict preemption' has been uniformly rejected every time it has been brought within the Seventh Circuit [collective cases]." App. 63. The district court nonetheless reviewed the evidence, as well as the preemption standard outlined in *Levine*, and held:

> As the record currently stands [], GSK has failed to meet its demanding burden of demonstrating by clear evidence that the FDA would have rejected a Paxil-specific adult suicide warning had GSK taken the FDA up on its request to schedule a formal meeting or submit a separate supplement to add the Paxil-specific adult suicide warnings.

App. 64-65. The case then proceeded to trial on plaintiff's negligent failure to warn claim. During the five-week trial, testimony was presented by a myriad of medical witnesses and experts, including:

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479 Mass. 141, 157 (2018) (Massachusetts); *but see McNair v. Johnson & Johnson*, 241 W. Va. 26 (2018) (refusing to find brand-name liability under West Virginia law).

Dr. Ross, an FDA expert who worked at the FDA for a decade in various capacities, including as deputy director of the Office of Drug Evaluation at the FDA's Center for Drug Evaluation and Research. Dr. Ross testified for four days. He testified concerning GSK's interactions with the FDA and various deficiencies in GSK's paroxetine label relative to adult suicide risks. Dr. Ross testified that, based upon his knowledge and experience, GSK could have utilized the CBE provision to issue a paroxetine-specific adult suicide warning in multiple sections of the label (outside of the class label). Dr. Ross testified that GSK was never prohibited from doing so by the FDA. App. 47 & 53-54; *see also* R.629, Tr.*889:3-984; R.630, Tr.*985-1112:12; R.623, Tr.*1122:12-1236; R.624, Tr.*1237-1345; R.625, Tr.*1346-1464; R.626, Tr.*1465-1574:9; R.627, Tr.*1618:20-1656:22.

The jury also heard from Dr. David Healy, a professor of psychiatry in the United Kingdom and an expert in pharmacological psychiatric treatment and research. Dr. Healy has written more than 200 peer-reviewed medical journal articles specifically relating to pharmaceutical medications of which 50 specifically related to the relationship of psychotropic medications and suicide. App. 48-49; *see also* R.617, Tr.*182:15-184:7. Dr. Healy has been a consultant to most of the major antidepressant manufacturers at some point in his life, including GSK, and has been studying the issue of Paxil-induced suicidality for well over 20 years. *Id*. Dr. Healy testified extensively (over a three-day period) concerning the causative association between

paroxetine and suicide in adult patients, his review of the clinical trials of Paxil, including GSK's original NDA submission as well as GSK's and the FDA's 2006 analyses, other types of evidence showing a causative association between Paxil and suicide, his clinical experience with drug-induced suicidality, the scientific literature, and the mechanisms by which paroxetine induces suicidal behavior. App. 46-49; *see also* R.617, Tr.*178:20-219; R.618, Tr.*220-342; R.619, Tr.*343-477; R.620, Tr.*478-611; R.621, Tr.*612-750; R.622, Tr.*751-862.

In addition, the jury heard from Joseph Glenmullen, M.D., a board-certified psychiatrist and clinical instructor at the Harvard Medical School who has published two books concerning the risks, including suicide risks, associated with antidepressants, including paroxetine. App. 49-50; *see also* R.632, Tr.*1897:8-1899:6. Dr. Glenmullen reviewed Mr. Dolin's medical records, reviewed the deposition testimony of the various doctors, treaters, family members and witnesses in this case and performed a differential diagnosis of Mr. Dolin's symptoms and behavior during the last week of his life and concluded that Mr. Dolin's suicide resulted from drug-induced akathisia caused by the ingestion of paroxetine. App. 49; *see also* R.632, Tr.*1896:15-1974; R.633, Tr.*1975-2083; R.634, Tr*2084, 2020; R.635, Tr.*2221-2324:3.

At the conclusion of the case and relying upon the Third Circuit's decision *In re Fosamax (Alendronate Sodium) Prod. Liab. Litig*., 852 F.3d 268, 272 (3d Cir. 2017), *cert. granted sub nom. Merck Sharp & Dohme*

*Corp. v. Albrecht*, 138 S. Ct. 2705 (2018), the district court concluded that the affirmative defense of federal preemption as set forth in *Levine* (whether GSK had presented clear evidence the FDA rejected or would have rejected an adult suicide warning), is a factual question for the jury. App. 35-36. The district court offered to submit the question to the jury with an appropriate instruction premised upon *Levine*. *Id*. GSK, however, took the position that preemption is a question of law and declined to have its affirmative defense submitted to the jury in the form stated in the court's proposed instruction. App. 36; *see also* R.665, Tr.*4244:17-22, *4244:3-4250:22.

After hearing the testimony of all the witnesses, including Mr. Dolin's prescribing physician, his other medical treaters, co-workers, clients, a nurse who observed the suicide, Mr. Dolin's family members, various expert witnesses and a GSK company representative, the jury deliberated for three days, submitted requests to see a number of exhibits, including all of the correspondence between GSK and the FDA concerning class labeling (R.654, Tr.*4486:9-12) and GSK's 2006 meta-analysis (R.655, Tr.*4493:3-4494:10), and returned a verdict of $3 million in favor of Wendy Dolin, for the death of her husband, Stewart Dolin. App. 31.

GSK moved for judgment as a matter of law and for a new trial based on various issues, including its contention that plaintiff's claims were preempted by federal law because the FDA refused or would have refused an adult suicide warning. App. 36 & 52-55. The district court, after reviewing the evidence presented

in the case and the relevant case law, including *Levine* and its progeny and post-*Levine* preemption decisions involving paroxetine, *rejected* GSK's preemption argument. The district court held that "[t]here is not clear evidence that the FDA would have rejected a Paxil-specific warning outside of the class warning." App. 55.

GSK then appealed to the Seventh Circuit, again raising its preemption defense. The Seventh Circuit reversed the district court's rulings, holding that "federal law prevented GSK from adding a warning about the alleged association between paroxetine and suicides in adults." The judgment was reversed and the case dismissed. App. 4.

In its ruling, the Seventh Circuit conceded that, in 2006, GSK "found evidence of an increase in suicide attempts in adults with major depressive disorder treated with paroxetine compared with placebo . . . [and] . . . that its data showed a 6.7-fold increase in suicide attempts in adults treated with paroxetine compared to a placebo." App. 11. The court further recognized that, without any repercussion, GSK unilaterally revised its paroxetine label in 2006, pursuant to the CBE provision, to warn of the adult suicide risk. App. 12. However, because GSK revised its label at a time when the FDA was reviewing antidepressant suicide data generally and the FDA subsequently requested a "class-wide" suicide warning for all antidepressants (which did not include the paroxetine-specific risks and only extended the suicide risk to young adults), the Seventh Circuit ruled this constituted "clear evidence" that GSK's paroxetine-specific

adult suicide warning was rejected in favor of the class-wide suicide warning. App. 12-15 & 22-26. The Seventh Circuit also recognized that "[t]he FDA advised GSK to submit the paroxetine-specific warning as a separate CBE," which GSK was statutorily permitted to do unilaterally without any invitation from the FDA. App. 14, 69 & 117.[3] Nonetheless, the Seventh Circuit construed the FDA's invitation to do something that GSK was legally permitted to do unilaterally and without invitation, as clear evidence of a rejection.

On the issue of whether the determination of clear evidence is a factual question for the jury or a legal question for the court, and if it is a factual question, what the standard of review should be, the Seventh Circuit opined that preemption usually is a legal question but recognized the Third Circuit in *In re Fosamax* held that the ultimate question of whether the FDA would have rejected a warning is a factual question for the jury. App. 21. Ultimately, the Seventh Circuit did not determine whether it is a factual question or a legal question and instead held that, even if it were a factual question for the jury, "no reasonable jury could find that the FDA would have approved an

[3] The Seventh Circuit states that "GSK submitted the CBE supplement that the FDA requested" (App. 14), however, that is factually incorrect. After May 2007, GSK merely submitted the class-warning which FDA had ordered all manufacturer's to incorporate—GSK *did not* comply with the FDA's request to submit a supplement that included the paroxetine-specific adult suicide warning in a separate supplement in addition to the class-warning (something it was free to do even without the FDA's request or invitation).

adult-suicide warning for Paxil under the CBE regulation between 2007 and Steward Dolin's suicide in 2010." App. 22. The Seventh Circuit thus concluded that the nine jurors who found in favor of Mrs. Dolin, the Honorable James B. Zagel, who initially denied GSK's preemption motion on summary judgment (App. 63-65), and the Honorable William T. Hart who denied GSK's preemption arguments when raised in GSK's reserved motion for judgment as a matter of law (App. 54-55), were all collectively unreasonable. Completely absent from the Seventh Circuit's ruling was *any* mention of the presumption against preemption, nor was there any discussion of the standard for reviewing motions for judgement which required the Court to view the evidence in a light most favorable to Mrs. Dolin as the non-moving party and to draw all reasonable inferences in Mrs. Dolin's favor.

Mrs. Dolin filed a timely petition for rehearing and rehearing *en banc,* which was denied. *See* App. 67-68.



## REASONS FOR GRANTING THE WRIT

### I. The Court Should Hold This Petition Pending Its Opinion in *Merck v. Albrecht*

Because the Court's resolution in *Albrecht* likely will provide guidance to the court below, the Court should hold this petition and then vacate and remand to the Seventh Circuit for further proceedings in light of *Albrecht*.

The Seventh Circuit's decision in this case directly conflicts with the Third Circuit's decision in several respects.

*First*, the Third Circuit determined that this Court intended to announce a "standard of proof" when it used the "clear evidence" standard for the preemption defense in *Levine* and concluded that, "for a defendant to establish a preemption defense under [*Levine*], the factfinder must conclude that it is highly probable that the FDA would not have approved a change to the drug's label." *See In re Fosamax*, 852 F.3d at 284-286. The Third Circuit further held that "the question of whether the FDA would have approved a plaintiff's proposed warning is a question of fact for the jury." *Id*. at 293. The Seventh Circuit did not determine whether the clear evidence requirement constitutes a standard of proof. Moreover, while the district court below found the Third Circuit's *In re Fosamax* highly persuasive and "offered to submit the question [of preemption] to the jury with an appropriate burden of proof instruction" *see* App. 35-36, GSK declined to have its affirmative defense submitted to the jury. *Id*. On appeal, Mrs. Dolin argued that, because GSK had refused the district court's offer to have its preemption defense submitted to the jury, it waived this defense. However, the Seventh Circuit never addressed the waiver argument. To the extent this Court in *Albrecht* answers the question of whether the *Levine* clear evidence standard is a standard of proof and, if such a factually intensive preemption question should be decided by the jury as the finder of fact, then this certainly will have a

substantial bearing on petitioner's case given the district court below was poised to follow *In re Fosamax* and submit the preemption issue along with an appropriate burden of proof instruction to the jury, but GSK rejected the Court's invitation and thus waived its defense. *See*, *e.g., Sims v. Mulcahy*, 902 F.2d 524, 535-536 (7th Cir. 1990); *see also Wojciechowski v. Long-Airdox Div. of Marmon Grp., Inc*., 488 F.2d 1111, 1118 (3d Cir. 1973).

*Second*, the Third Circuit held that the appropriate inquiry is "whether a reasonable juror could find that it is *highly probable* that the FDA would have rejected the warning. Put differently: even if it seems possible or plausible that the FDA would have rejected the proposed warning, could a reasonable juror nonetheless conclude that the odds of rejection were something less than highly probable?" *In re Fosamax*, 852 F.3d at 295. The Seventh Circuit did not adopt this "highly probable" standard and thus this Court's determination of the appropriate applicable standard will be instructive to petitioner's case.

*Third*, in a factual pattern very similar to petitioner's case, which among other things included a manufacturer, Merck, that apparently proposed an enhanced warning which the FDA rejected via a "complete response" letter, the Third Circuit nonetheless applied the heightened clear evidence burden of proof and *drawing all reasonable inferences in plaintiffs' favor* concluded that a reasonable jury could have concluded that Merck could have issued enhanced warnings via the CBE process, *In re Fosamax*, 852 F.3d

at 297-298; that a reasonable jury could also conclude the FDA's previous rejection of Merck's enhanced warning was due to Merck's use of an inappropriate or watered-downed term ("stress fractures") to characterize the risk of atypical fractures, *id*. at 298-299; and once the FDA rejected Merck's enhanced stress fracture warning, "the ball was back in Merck's court to submit a revised, corrected proposal [and] a reasonable juror could therefore conclude that it was Merck's failure to submit a revised CBE . . . rather than FDA's supposedly intransigent stance on the science, that prevented FDA from approving a label change[,]" *see id.* at 299.

Unlike the Third Circuit's analysis as discussed above, the Seventh Circuit took a different path. Notably, while Petitioner's victory arose out of a jury verdict, as opposed to summary judgment, pursuant to Rule 50(a) and the case law as it applies to renewed motions for judgment as a matter of law, the appropriate standard that should have been implemented by the Seventh Circuit was to determine whether the evidence presented, combined with all reasonable inferences, is sufficient to support the verdict when viewed in the light most favorable to Mrs. Dolin as the nonmovant. *See* App. 36; *see also Reeves v. Sanderson Plumbing Products, Inc*., 530 U.S. 133, 150 (2000); *Dadian v. Vill. of Wilmette*, 269 F.3d 831, 837 (7th Cir. 2001). Unlike the Third Circuit, which appropriately drew all reasonable inferences and viewed the facts in a light most favorable to the plaintiffs, the Seventh Circuit appears to have lost sight of this mandatory standard. It

never once stated that it was duty bound to view the evidence and all reasonable inferences in a light most favorable to Mrs. Dolin, and instead, appears to have viewed the evidence and drawn all inferences in a manner most favorable to GSK.

Moreover, the Third Circuit determined the question of why the FDA rejected Merck's initial enhanced warning was a question for the jury to resolve and that a reasonable juror could determine the rejection was due to stylistic issues and not a rejection of the association between the actual serious risk of atypical fractures. *In re Fosamax*, 852 F.3d at 298-299. Unlike the Third Circuit, which permitted a reasonable jury to determine why a prior warning was rejected and whether it amounted to clear evidence of rejection, and notwithstanding the fact the district court and nine jurors rejected GSK's arguments that it was prevented from issuing an adult suicide warning, the Seventh Circuit held that the FDA-requested class suicide warning established as a matter of law that the FDA rejected and would have rejected any paroxetine-specific suicide warning. App. 22-26. In doing so, the Seventh Circuit disregarded without any explanation the expert opinion of plaintiff's FDA expert, Dr. David Ross. Dr. Ross reviewed the facts and, based on his knowledge and experience, testified (over the course of four days at trial) that the FDA never prohibited GSK from issuing a paroxetine-specific adult suicide warning and was free to utilize the CBE provision to include a paroxetine-specific warning in multiple locations

outside of the class label. App. 47 & 53-55; *see also* R.629, Tr.*889:3-984; R.630, Tr.*985-1112:12; R.623, Tr.*1122:12-1236; R.624, Tr.*1237-1345; R.625, Tr.*1346-1464; R.626, Tr.*1465-1574:9; R.627, Tr.*1618:20-1656:22.

The Seventh Circuit also disregarded the trial testimony of GSK's vice-president who admitted the FDA never told GSK that it was "prohibited from putting any Paxil-specific information anywhere in the label." R.645, Tr.*3375:16-19.

Finally, unlike the Third Circuit which held that, notwithstanding the FDA's rejection of a previous warning, a reasonable juror could conclude that "the ball was in Merck's court" to submit a revised CBE for the correct enhanced warning, *In re Fosamax*, 852 F.3d at 299, the Seventh Circuit rejected Petitioner's similar arguments, and apparently giving no weight to the FDA's communication to GSK telling GSK to submit a supplemental CBE concerning the paroxetine-specific adult suicide risks to be included after the class labeling had been implemented for all antidepressants on the market (App. 100). Likewise, the Seventh Circuit failed to weigh, in petitioner's favor, the opinions of the FDA expert, Dr. Ross, who opined that, after the implementation of the class warning, GSK remained free and indeed had a duty under the FDA rules and an invitation from the FDA to implement enhanced adult suicide warnings using the CBE procedure. App. 47 &

53-54.[4] In sum, whereas the Third Circuit properly applied *Levine* and properly viewed the evidence and all inferences in a light most favorable to the non-moving party, the Seventh Circuit reached a result that directly conflicts with the Third Circuit, conflicts with the appropriate standard of review and deference that should be afforded to the jury's verdict, and it is at odds with *Levine*. The likely effect of the Court's holding in *Albrecht* on these issues, warrants that the Court hold this petition, and then grant, vacate and remand for further proceedings in light of *Albrecht*.

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[4] For example, the Seventh Circuit stated that "GSK has provided *undisputed* evidence that the FDA rejected any adult-suicidality warning in 2007 when the agency required all SSRIs to adopt the same class-wide warning." App. 22 (emphasis added). Nothing can be further from the truth. During trial, the FDA expert, Dr. Ross, went through the regulatory files and FDA communications and testified at length, over the course of four days, that GSK was never prohibited from issuing a paroxetine-specific adult suicide warning, that FDA never rejected an adult suicide warning and GSK was free to utilize the CBE provision to unilaterally enhance its label to warn of paroxetine-specific adult suicide. He also went through the label and identified at least 11 different locations within the label where GSK could have issued such a warning. *See* App. 47 & 52-55; *see also supra* at 31 (citations to Dr. Ross' trial testimony). The Seventh Circuit's opinion neglects to even mention Dr. Ross' relevant testimony, indicating the court improperly viewed the evidence and reasonable inferences in a light most favorable to GSK as opposed to Dolin, erroneously ignored the evidence supporting petitioner and made impermissible credibility determinations.

## II. No Matter How the Court Decides *Albrecht*, this Case Provides an Ideal Vehicle to Further Define Important Contours of Preemption Analysis in Prescription Drug Cases

There are several issues of substantial importance in this case which are not involved, or only tangentially involved, in *Albrecht* which further warrant that petitioner's petition be granted.

*First*, as discussed *supra*, the relevant FDA labeling and CBE regulations (i.e., 21 C.F.R. 314.70) were revised in September 2008 and many of the relevant events that should have initiated a labeling change by GSK occurred prior to 2008, yet the Seventh Circuit improperly retroactively applied the 2008 statutory revisions. App. 6, 19. Paxil entered the market in 1992 and Mr. Dolin's suicide occurred in 2010. There is an 18-year time period in which GSK had the responsibility to monitor the adverse events associated with its drug and modify its label to properly warn of adult suicide risks. *Levine*, 555 U.S. at 569-570. Importantly, between 1992 and September 2008, the Code of Federal Regulations permitted GSK to use the CBE provision to unilaterally modify its label to strengthen its warnings *as GSK saw fit*. App. 69-70 & 117. In September 2008, the CBE regulations were amended to, *for the first time*, state that a manufacturer may only make unilateral changes to strengthen its label if it has "newly acquired information" evidencing a "causal association" with a risk. App. 118; 73 Fed.Reg. 49609 (2008); *see also Levine*, 555 U.S. at 568-569.

The Seventh Circuit committed a grave error by impermissibly applying the September 2008 CBE amendment *retroactively*, examining the period of 1992 through August 2008 as if the law required GSK to have "newly acquired information" of a "causal association" prior to being permitted to use the CBE to make a labeling change, *see* App. 19-20, when the law and the CBE regulations in effect between 1992 and September 2008 *did not* have such restrictions. App. 69-70 & 117. GSK's conduct, duties, opportunities and responsibilities under federal law should have been adjudicated based on the statutes and regulations as they existed at the relevant time. *Tucker v. SmithKline Beecham Corp*., 596 F.Supp. 2d 1225, 1236 (S.D. Ind. 2008) ("Regardless of what the FDA ordered in 2007, if GSK had evidence of a reasonable association between Paxil and adult suicidality in 2002, it had the duty then under the FDA's regulations to strengthen the warnings on Paxil's label.").

*Second*, two different district court judges in this case reviewed the events surrounding the 2007 class labeling change and concluded these facts do not establish that GSK was prohibited from issuing a paroxetine-specific adult suicide warning in the paroxetine label. App. 63-65 (J. Zagel); App. 54-55 (J. Hart). It is difficult to reconcile the panel's conclusion that "no reasonable jury could find that the FDA would have approved an adult-suicidality warning . . . " (App. 22) when nine jurors and two distinguished district court judges reviewing these same facts found that GSK was not prohibited from issuing stronger warnings.

Moreover, the unreasonableness of the Seventh Circuit's ruling is highlighted by the fact that, even its lead author, Hon. David F. Hamilton, when he was a district court judge, held in a case involving an adult Paxil suicide, that the failure to warn claims against GSK were not preempted and that the FDA's actions and interactions with GSK vis-à-vis the class suicide label did not justify a finding of preemption:

> [I]n spite of the FDA's direction regarding Paxil's label in May 2007, GSK still had (and has) the obligation to revise its label to strengthen a warning upon reasonable evidence of an association of a serious hazard, particularly with respect to this individual drug . . . In other words, the FDA's revisions were not necessarily the final word on Paxil's label and did not put GSK into a position where it was impossible for GSK to comply with both state and federal law.

*Tucker*, 596 F.Supp. 2d at 1235-1236 (J. Hamilton). Post-*Levine*, courts have also analyzed GSK's preemption argument and refused to find preemption:

> In denying the proposed language, the agency did not prohibit all enhanced warnings. Instead, the FDA merely required removal of Paxil-specific language from a particular portion of Paxil's label in favor of uniform class-wide labeling for all SSRI's. The agency's action did not preclude Paxil-specific language changes to other areas of the labeling or prevent GSK from pursing a label change

> through submission of a separate supplement.

*Forst v. SmithKline Beecham Corp.*, 639 F.Supp. 2d 948, 954 (E.D. Wis. 2009).

*Third*, the Seventh Circuit misconstrued the "clear evidence" standard of *Levine*. And, the panel's analysis of *Levine* conflicts with the Seventh Circuit's earlier analysis of *Levine* as articulated in *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387 (7th Cir. 2010). *Mason* held that, to understand the "clear evidence" standard, one must view *Levine* "as whole" which includes portions of the *Levine* dissent's un-conflicted recitation of the administrative history of Phenergan. *Mason*, 596 F.3d at 391-393. A close reading of *Levine* reveals that, for decades, the FDA had focused specifically on the safety of the IV-push administration of Phenergan, the FDA rejected a request to ban such use and the "FDA strongly considered a similar warning to the one the plaintiff proposed" but it was rejected by the FDA. *Mason*, 596 F.3d at 393 (discussing *Levine*). *Mason* then went on to note that, even under these extreme facts, the Supreme Court nonetheless still refused to find preemption. *Id.*[5] Here, as outlined *supra*,

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[5] In *Levine*, the majority noted that, in the late 1980s when Wyeth used the CBE provision to make a labeling change to issue further warnings regarding the specific use and injury at issue in that case, the FDA rejected the label changes and was instructed to "retain verbiage in current label." *Levine*, 555 US at 562. Moreover, in commenting on the dissent's recitation of the facts, the majority concluded that "*even the dissent's account does not support the conclusion that the FDA would have prohibited Wyeth from adding a stronger warning pursuant to the CBE regulation*." *Levine*, 555 U.S. at 573, n.6 (emphasis added).

there is no evidence the FDA ever rejected a paroxetine-specific adult suicide warning. The FDA's invitation to GSK to use the CBE (which GSK could use unilaterally without the FDA's invitation) to issue a paroxetine-specific adult suicidality warning in a place within the label that is outside the class labeling section can hardly be considered or interpreted as a rejection of a paroxetine-specific adult suicide warning. Indeed, it is surprising that, in light of *Levine* as well as *Mason*'s interpretation of the "extensive showing" required under *Levine*, that the panel has construed the FDA's *invitation* to GSK to submit a separate CBE as clear evidence of a *rejection* of the suicide warning. It is akin to being invited to dance but construing that invitation as clear evidence of rejection.

Finally, GSK's preemption defense (i.e., federal law prohibits it from issuing a truthful warning) should be adjudicated against the backdrop of the First Amendment. *Thompson v. Western States Medical Center*, 535 U.S. 357, 365 (2002). GSK has a First Amendment right to engage in truthful speech and the public has a First Amendment right to receive such information. *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 756 (1976); *see also Board of Trustees of Leland Stanford Junior University v. Sullivan*, 773 F.Supp. 472, 474 (D.D.C. 1991) ("[T]the First Amendment protects scientific expression and debate just as it protects political and artistic expression."). The dissemination of truthful safety information containing "factual material of clear 'public interest'" is entitled to First Amendment protection. *Bigelow v. Virginia*, 421 U.S. 809, 822

(1975); *Riley v. Nat'l Fed'n of the Blind of N. Carolina, Inc*., 487 U.S. 781, 791 (1988).

The Seventh Circuit's decision creates a world where a drug manufacturer is *permitted* under the First Amendment to promote its drug for non-FDA approved indications, which would normally be a violation of the FDCA, *United States v. Caronia*, 703 F.3d 149, 154 (2nd Cir. 2012), but a drug manufacturer is *prohibited* from issuing warnings concerning life threatening risks associated with its drug, *see* App. 4. The FDCA regulations, which were designed to be a weapon of the public against drug manufacturers to ensure they deliver safe drugs and appropriate warnings, have now been turned into a weapon against the public.

## CONCLUSION

The petition for writ of certiorari should be held pending the Court's decision in *Albrecht*, after which the Court should grant the petition, vacate the judgment below, and remand for reconsideration in light of *Albrecht*. In the alternative, the Court should grant the petition and schedule the case for briefing and hearing on the merits.

Respectfully submitted,

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