No. 22-1180

IN THE

Supreme Court of the United States

SHIRE US INC.; SHIRE LLC,

Petitioners,

v.

MARK BLACKBURN,

Respondent.

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

RESPONDENT'S BRIEF IN OPPOSITION

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QUESTION PRESENTED

Whether an unpublished, non-precedential decision reflecting a straightforward application of *Wyeth v. Levine*, 555 U.S. 555 (2009), and relevant regulations warrants review.

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INTRODUCTION

After suffering serious kidney disease associated with the drug Lialda, respondent Mark Blackburn sued the drug's manufacturer, petitioner Shire US and related entities, for failure to warn under Alabama law. His complaint alleges that Shire's labeling for Lialda was inadequate because the Warnings and Precautions section of the labeling failed to provide information about periodic testing necessary to protect against renal harm. As this Court has recognized, federal regulations allow drug manufacturers to update their products' labeling, without prior approval, to strengthen warnings and precautions. *See Wyeth v. Levine*, 555 U.S. 555, 568 (2009). And as the Court has held, a state-law failure-to-warn claim against the manufacturer of a prescription drug is not preempted absent clear evidence that the Food and Drug Administration (FDA) would not have approved a labeling change to include the warning. *Id.* at 571–72. Accordingly, both the district court and the Eleventh Circuit rejected Shire's argument that Mr. Blackburn's failure-to-warn claim is preempted.

The decision below is a straightforward application of *Wyeth* and FDA regulations. Perhaps for that reason, the Eleventh Circuit issued a short, non-precedential opinion.

Skimming over the preemption argument actually made and addressed below, the petition characterizes the opinion as saying something that it does not: that Shire could have made changes to the Highlights section of the drug's labeling without prior FDA approval. That is not what Mr. Blackburn argued or what the court of appeals held. In particular, nothing in the Eleventh Circuit's opinion requires Shire, or

any other drug manufacturer, to make changes to the Highlights section of its labeling in order to avoid liability for failure to warn. Rather, like a typical failure-to-warm claim concerning a prescription drug, Mr. Blackburn's claim concerns the inadequacy of the Warnings and Precautions section, and the decision below does no more than allow his claim to proceed to trial. Consistent with the claim alleged and the parties' arguments on appeal, the court of appeals' unremarkable decision presents no question worthy of this Court's review.

STATEMENT

A. Regulatory Background

Since 1938, the manufacturer of a new prescription drug must obtain prior approval from the FDA before the drug can be marketed. To obtain marketing approval, a drug company must first submit a new drug application for the FDA's review. 21 U.S.C. §§ 355(a), (b). If, after reviewing the application, the FDA concludes that the drug is safe and effective for its intended use or uses and that the labeling is not false or misleading, the FDA will send an approval letter to the applicant. *Id.* §§ 355(c)(1)(A), 355(d).

FDA approval includes approval of the labeling. The majority of the labeling is referred to as the "Full Prescribing Information," which includes sections stating directions for use, contraindications, warnings, precautions, and adverse reactions, among other things. *See* 21 C.F.R. §§ 201.56, 201.57, 201.80. The labeling also includes a "Highlights" section, which summarizes the content of the Full Prescribing Information, *id.* § 201.57(b), but unlike the Full Prescribing Information, does "not include all the

information needed to use [the drug] safely and effectively," *id*. § 201.57(a)(1).

Unfortunately, "[m]any serious [adverse drug reactions] are discovered only after a drug has been on the market for years." Karen Lasser, et al., *Timing of New Black Box Warnings and Withdrawals for Prescription Medications*, 287 J. Am. Med. Ass'n 2215, 2218 (May 1, 2002); *see* Jean Lester, et al., *Evaluation of FDA safety-related drug label changes in 2010*, 22 Pharmacoepidemiology and Drug Safety 302, 304 (2013) (stating that "[t]he most critical safety-related label changes" were made "a median 10 and 13 years after drug approval"). To monitor adverse reactions, the FDA requires companies to submit "adverse event reports" to the agency describing both "serious and unexpected" reactions and less serious ones. *See* 21 C.F.R. §§ 314.80(c)(1), (2). In this way, federal regulations put the onus of postmarketing surveillance on drug manufacturers, not the FDA.

Federal regulations also impose on manufacturers a continuing responsibility "to maintain their labeling and update the labeling with new safety information." *Wyeth*, 555 U.S. at 571 (quoting 73 Fed. Reg. 49603, 49605 (Aug. 22, 2008)); *see id*. (quoting 21 C.F.R. § 201.80(e) (requiring a manufacturer to revise labeling "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug")). A manufacturer can make certain post-approval labeling changes—including most changes to Highlights—only with prior FDA approval. *See* 21 C.F.R. § 314.70(b). Prior approval is *not* required, however, for changes "[t]o add or strengthen a contra-indication, warning, precaution, or adverse reaction," *id*. § 314.70(c)(6)(iii), among other things, *id*. §§ 314.70(c), (d). Section 314.70(c) is

often referred to as the "CBE" process, because it allows the manufacturer to inform the FDA of "changes being effected." *See Wyeth*, 555 U.S. at 568, 570. A company's obligation to provide physicians and patients with up-to-date warnings and precautions continues as long as the product is marketed. 21 C.F.R. §§ 201.57(c)(6), 201.80(e).

In light of the regulatory scheme, and reinforced by the reality that manufacturers initiate the majority of labeling updates, this Court held in *Wyeth*—and reaffirmed in *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019)—that FDA approval of prescription drug labeling does not immunize a brand-name drug manufacturer from liability for failure to warn. Rather, "absent clear evidence that the FDA would not have approved a change to [the] label" to include the warning, the Court "will not conclude that it was impossible for [the manufacturer] to comply with both federal and state requirements." *Wyeth*, 555 U.S. at 571. And absent an "affirmative decision" by the FDA, such clear evidence is lacking. *Id*. at 572.

B. Factual Background

1. In January 2007, the FDA approved Shire's new drug application for Lialda, a mesalamine drug, to treat ulcerative colitis. Pet. App. 7, 72. Mesalamine drugs pose a risk of kidney disease. *Id*. 52. Originally, Shire's labeling for Lialda stated in Section 5.1, "Warnings and Precautions": "Reports of renal impairment … have been associated with mesalamine medications and pro-drugs of mesalamine." First Am. Compl. ¶ 17. Later, at the FDA's request, the labeling was revised to note the possibility of "renal failure." *Id*. ¶ 18; Pet. App. 7. To identify potential kidney disease and prevent severe impairment, Lialda's

labeling recommended "that patients have an evaluation of renal function prior to initiation of LIALDA therapy and periodically while on therapy." First Am. Compl. ¶ 18 (2013 warning); Pet. App. 53.

Between Lialda's approval in 2007 and November 2013, a growing body of medical literature documented renal toxicity of mesalamine in the treatment of ulcerative colitis and Crohn's disease and suggested the need for monthly testing of renal function. Pet. App. 5–6; *see* First Am. Compl. ¶¶ 86–88. For example, an "article from 2009 recommended" that a "monthly monitoring schedule … should have been part of Shire's warning." Pet. App. 6. Shire also received adverse event reports of renal impairment associated with use of Lialda during this period. *Id*. Nonetheless, during this period, Shire revised Lialda's labeling "in only one significant way"—to add "renal failure" to the warnings section, after the FDA requested that change. *Id*. 7. Otherwise, Shire has not "attempted to strengthen the monitoring instruction" for renal impairment or failure. *Id*.

2. In November 2013, Mark Blackburn's gastroenterologist in Huntsville, Alabama diagnosed him with Crohn's disease and prescribed Lialda. *Id*. 52. His physician interpreted Lialda's labeling recommendation to "periodically" evaluate a patient's renal function to mean evaluation once a year. *Id*. 16, 53. Although Mr. Blackburn scheduled a follow-up appointment for two months after he was prescribed Lialda, the appointment was canceled. *Id*. 53. In any event, "[e]ven if Blackburn had kept the appointment, it is unlikely [his physician] would have ordered blood work to evaluate kidney function" because his standard practice was to periodically test for renal function after "about a year" of treatment. *Id*.

About one year after starting Lialda, Mr. Blackburn moved to Birmingham. His original physician continued to refill Mr. Blackburn's prescriptions, and Mr. Blackburn's renal function went unmonitored. *Id*. 52. A few months later, Mr. Blackburn stopped taking the drug. "In all, Blackburn took LIALDA for somewhere between 12 and 16 months." *Id*. 54.

In April 2015, a blood test revealed an excessive amount of creatinine, and a nephrologist, Dr. Agata Przekwas, diagnosed Mr. Blackburn with advanced chronic interstitial nephritis—a type of kidney disease that manifests as irreversible scarring and diminished kidney function. Mr. Blackburn's kidney disease was stage four, meaning that his kidneys were functioning at approximately 20 percent of their normal capacity. He is currently awaiting a kidney transplant. *Id*.

Both Dr. Przekwas and Dr. Jonathan Winston, a nephrology expert retained by Mr. Blackburn, concluded that Mr. Blackburn's injuries were preventable and that the kidney disease could have been detected at least six months before it was diagnosed and possibly as early as August 2014. *Id*. Had Mr. Blackburn stopped taking Lialda at that time, Dr. Winston concluded, his kidney function "would be either normal or near normal." *Id*.

C. District Court Proceedings

Mr. Blackburn sued Shire in June 2016, asserting four claims under Alabama law. Only the failure-to-warn claim is at issue here.

The failure-to-warn claim alleges that the drug's labeling contained an inadequate warning regarding its potential renal toxicity. *Id*. 55–56, 93–94. The

complaint alleges that the Full Prescribing Information portion of the Lialda labeling should have instructed prescribers to "evaluat[e] ... renal function by a simple serum (blood) test of creatinine levels on a monthly basis for the first three months after initiation of therapy and then on a quarterly basis for at least one year." *Id.* 56; *see also* First Am. Compl. ¶¶ 5, 24. The timing specified in the complaint is based on the labeling used in the United Kingdom and on an expert declaration. The failure-to-warn claim specifies that Mr. Blackburn's physician both reviewed and relied on the "Warnings and Precautions" in the Full Prescribing Information, First Am. Compl. ¶¶ 157–58; it does not mention the Highlights section of the labeling, *see id.* ¶¶ 149–70.

Shire moved to dismiss the claim arguing, among other things, impossibility preemption based on the theory that it lacked the ability to revise the labeling. After discussing the regulatory scheme and this Court's decision in *Wyeth v. Levine*, 555 U.S. 555 (2009), *see* Pet. App. 119–21, the district court rejected the argument. As the court explained, there is no impossibility preemption because, "[t]o the extent that Plaintiff's Amended Complaint seeks relief for an alleged defect in the [Full Prescribing Information] warning, there is no preemption at this stage of litigation, because Plaintiff has plausibly pled that Defendants could have utilized the CBE process." *Id.* 127–28.

After further proceedings, Shire moved for summary judgment. The court granted the motion, holding that Mr. Blackburn had failed to show that the labeling's alleged inadequacies actually or proximately caused his injuries. *Id.* 57.

D. Appeal and Certification to the Alabama Supreme Court

Mr. Blackburn appealed, and the Eleventh Circuit reversed. *Id.* 61–62. The court held that, considering his physician's testimony and drawing all inferences in Mr. Blackburn's favor, genuine issues of material fact exist concerning causation and that a reasonable jury could find that Mr. Blackburn's physician would have read and heeded a labeling that warned of a need for more frequent testing. *Id.* 62–66.

As an alternative basis to affirm the grant of summary judgement, Shire argued that the district court erred in recognizing Mr. Blackburn's theory of liability as a matter of Alabama law. In response, the Eleventh Circuit certified two questions to the Supreme Court of Alabama: whether under Alabama law "a pharmaceutical company's duty to warn [may] include a duty to provide instructions about how to mitigate warned-of risks," and whether "a plaintiff [may] establish that a failure to warn caused his injuries by showing that his doctor would have adopted a different course of testing or mitigation, even though he would have prescribed the same drug." *Id.* 11. The Supreme Court of Alabama answered both questions in the affirmative. *Id.* 34–35.

The case then returned to the Eleventh Circuit where the one remaining issue was Shire's impossibility preemption argument. In an unpublished, non-precedential opinion, the court held that Mr. Blackburn's failure-to-warn claim is not preempted. *Id.* 8.

The Eleventh Circuit began its preemption analysis by noting that federal law preempts state law when it is "impossible for a private party to comply

with both state and federal requirements." *Id.* 3–4 (quoting *Albrecht*, 139 S. Ct. at 1672). "[T]he possibility of impossibility is not enough." *Id.* 4 (quoting *Albrecht*, 139 S. Ct. at 1683 (Thomas, J., concurring) (cleaned up)).

Citing *Wyeth*, *Albrecht*, and FDA regulations, the court then described the regulatory scheme and, in particular, a manufacturer's ability to revise its product labeling without FDA approval to "add or strengthen a contraindication, warning, [or] precaution." *Id.* (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A)). The court explained that, "[b]ecause the 'changes-being-effected' regulation permits label changes, 'a drug manufacturer will not ordinarily be able to show that there is an actual conflict between state and federal law such that it was impossible to comply with both.'" *Id.* 5 (quoting *Albrecht*, 139 S. Ct. at 1679). Rather, "[i]mpossibility preemption exists only where there is 'clear evidence that the FDA would not have approved a change.'" *Id.* (quoting *Wyeth*, 555 U.S. at 571). And "[w]hether 'clear evidence' exists is a 'matter of law for the judge to decide.'" *Id.* (quoting *Albrecht*, 139 S. Ct. at 1679).

Noting that its review was "circumscribed by the standard for summary judgment," the court concluded that the failure-to-warn claim is not preempted. *Id.* 6. The court found that sufficient evidence existed in the record—including "a growing body of medical literature" and "reports of renal impairment that Shire received between the label's initial approval and Blackburn's injury"—to support "the basis for seeking a label change" to include a stronger monitoring instruction. *Id.* Moreover, the record lacked "clear evidence" of impossibility, because the FDA "never indicated that it would not have accepted the change."

Id. Indeed, Shire never contended that "it ever attempted to strengthen the monitoring instruction" pursuant to the "changes-being-effected regulation," which "places the onus on the manufacturer to 'ensur[e] that its warnings remain adequate as long as the drug is on the market.'" *Id*. 7 (quoting *Wyeth*, 555 U.S. at 570–71).

Finally, the Eleventh Circuit addressed Shire's argument that a change to the Full Prescribing Information regarding renal evaluation was impossible because a CBE would require a change to the Highlights as well. As Mr. Blackburn's brief had pointed out, Shire's theory would effectively bar use of the CBE process to update Warnings in drug labeling. Rejecting Shire's argument, the court of appeals recognized that the Highlights summary cannot be revised through the CBE process, *see id*., but also reiterated that the CBE process remains available for manufacturers to revise the Warnings section "to increase the safe use of the drug product," *id*. 8 (quoting 21 C.F.R. § 314.70(c)(6)(iii)(C)). As the court explained, "Blackburn's proposed language fits into [the latter] category because it is a recommendation for how to administer LIALDA in a way that increases its safe use." *Id*.

Shire filed a petition for rehearing or rehearing en banc. No member of the court called for a vote, and the petition was denied. *Id*. 9–10.

REASONS FOR DENYING THE WRIT

I. The decision below poses no conflict with case law or FDA regulations.

Shire's assertion that the decision below "departs" from the understanding of "numerous courts," Pet. 24, fails for two independent and equally important

reasons. To begin with, the Eleventh Circuit's unpublished decision is "not considered binding precedent." 11th Cir. R. 36-2. A non-precedential opinion simply cannot place manufacturers in the "damned-if-you-do, damned-if-you-don't position" that Shire purports to worry about. Pet. 26.

Furthermore, Shire's assertion depends on a mischaracterization of Mr. Blackburn's claim and the decision below. Mr. Blackburn's complaint does *not* challenge the content of the Highlights section; it focuses on the "Warnings and Precautions" section. First Am. Compl. ¶¶ 18, 157–58. None of the four appellate decisions cited by Shire, Pet. 25, involves the Highlights section; three of the four do not involve labeling at all. And none of the four, or indeed any other, holds that a manufacturer is barred from revising Warnings and Precautions through the CBE process without prior FDA approval for the change.[1]

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[1] Three of the four cases concern packaging, design defect, or manufacturing defect claims. *See Ignacuinos v. Boehringer Ingelheim Pharms. Inc.*, 8 F.4th 98, 103 (2d Cir. 2021) (concluding that "the plaintiffs' state law design and manufacturing defect claims are preempted to the extent that they would require any change listed in [21 C.F.R.] § 314.70(b)(2)"); *Gustavsen v. Alcon Labs., Inc.*, 903 F.3d 1, 11 (1st Cir. 2018) (stating that "[t]he change urged by plaintiffs to the product dispensing bottle fits comfortably into the" categories defined as "major"); *Yates v. Ortho-McNeil-Janssen Pharms., Inc.*, 808 F.3d 281, 298 (6th Cir. 2015) (stating that a design change is a "major" change and holding that a "design defect claim" is preempted). The fourth case, involving a claim by a brand-name drug manufacturer that a generic drug product was misbranded, does not concern or mention the Highlights section. *See Schering-Plough Healthcare Prods., Inc. v. Schwarz Pharma, Inc.*, 586 F.3d 500 (7th Cir. 2009).

Instead, each of the four decisions Shire cites stands for the undisputed point that the CBE process is not available for "major" changes. FDA regulations make that point explicitly: Section 314.70(b) defines "changes requiring … approval prior to distribution of the product made using the change" as "major changes." The regulations are also clear that changes to "add or strengthen a contraindication, warning, [or] precaution" are *not* "major" changes and *are* permitted through the CBE process, without FDA pre-approval. 21 C.F.R. § 314.70(c)(6)(iii)(A).

Shire's contention that the Eleventh Circuit is an outlier depends on its assertion that the court stated that a manufacturer can revise the Highlights section of the labeling through the CBE process. That argument misreads the Eleventh Circuit's decision and ignores the briefing to which the decision responds. Shire's beef is with one paragraph at the end of the opinion:

> We further reject Shire's alternative argument that it was precluded from changing the warning because it was contained in the "Highlights" section of the LIALDA label. *See* 21 C.F.R. § 314.70(b)(2)(v)(C) (2016). The relevant regulation states that "[a] supplement must be submitted for" three categories of "labeling changes." *Id.* §§ 314.70(b)(1), (b)(2)(v). Shire focuses on subsection (b)(2)(v)(C), which requires a supplement for "[a]ny change to the information required by" the Highlights section, 21 C.F.R. § 201.57(a). But Shire overlooks subsection (b)(2)(v)(A), which exempts "[c]hanges in labeling ... described in paragraph[ ] (c)(6)(iii)." *Id.* § 314.70(b)(2)(v)(A). Subsection (c)(6)(iii), of course, is the very

> subsection at issue here, regarding "changes-being-effected." And one of the categories in the "changes-being-effected" regulation permits "add[ing] or strengthen[ing] an instruction about dosage and administration that is intended to increase the safe use of the drug product." *Id*. § 314.70(c)(6)(iii)(C). Blackburn's proposed language fits into that category because it is a recommendation for how to administer LIALDA in a way that increases its safe use.

Pet. App. 7–8. Although Shire construes that paragraph to hold that manufacturers may make CBE changes to the Highlights section, that is not what the opinion says. It says that the language that Mr. Blackburn alleges that Shire failed to include "fits into [the] category" of changes for which a CBE change is permissible. That conclusion is correct: Mr. Blackburn's claim is based on the inadequacy of the Warnings and Precautions in Section 5.1 of the Full Prescribing Information, which is commonly revised using the CBE process. Nothing in the opinion suggests that the court believed that Mr. Blackburn's claim concerned the content of the Highlights. In fact, in discussing the facts and preemption arguments before turning to Shire's "alternative argument" at the very end of the opinion, the court does not even mention the Highlights section.

To the extent that the brevity of the one paragraph in the unpublished, non-precedential decision allows for any ambiguity, the complaint and the appellate briefing make the holding clear. In the complaint, the failure-to-warn claim does not mention the Highlights section; rather, it specifies the inadequacy of the Warnings and Precautions, First Am. Compl. ¶¶ 149–

70—a section to which CBE changes are permitted. Shire's appellate brief reflects that it correctly understood the claim.

The paragraph with which Shire now takes issue responds to an alternative argument in Shire's appellate brief: that it was barred from making CBE changes to the Warnings and Precautions because doing so would require changes to the Highlights that could not be made without FDA approval. According to Shire, because Highlights must reflect "the same information" as the Full Prescribing Information, Appellee Br. 51, "the change plaintiff contends should have been made would impact" Highlights, as well as the Full Prescribing Information. *Id*. 50–51. In addition, Shire argued that both recommendations about patient monitoring and any revisions to the warnings and precautions must appear in the Highlights, thereby precluding CBE changes to those topics in the Full Prescribing Information. *Id*. 51.

In response, Mr. Blackburn made several points. First, he pointed out that the Highlights section is by definition a *summary* of the full labeling. Indeed, the FDA requires the Highlights section to state: "These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product)." 21 C.F.R. § 201.57(a)(1); *see* Appellant's Reply 22–23; *see also* FDA, *Guidance for Industry: Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* at 13 (Feb. 2013) (stating that "not all of the safety information from the [Full Prescribing Information] will always be included in

Highlights");[2] Pet. 6 (explaining that the Highlights section "contains a summary" (quoting 71 Fed. Reg. 3922, 3932 (Jan. 24, 2006))). And a CBE change to specify in the Full Prescribing Information that "renal function by a simple serum (blood) test of creatinine levels" should be evaluated "on a monthly basis for the first three months after initiation of therapy and then on a quarterly basis for at least one year," First Am. Compl. ¶ 25, would be consistent with, and hence require no change to, the statement in the Highlights summary advising physicians to evaluate renal function "periodically."

Indeed, the reply brief explained, if Shire were correct that new or revised Warnings and Precautions necessarily required changing the Highlights, the CBE process could never be used to provide new Warnings and Precautions or other important sections of the labeling, rendering the CBE provision—and this Court's decision in *Wyeth*—a nullity. Appellant's Reply 23–24; *see In re Testosterone Replacement Therapy Prods. Liab. Litig. Coordinated Pretrial Proc.*, 430 F. Supp. 3d 516, 529 (N.D. Ill. 2019) (declining to adopt this reading as inconsistent with *Wyeth* and noting that it "would prevent drug manufacturers from making significant safety- and efficacy-related label changes using the CBE process"). The CBE regulations, however, implement the requirement that manufacturers promptly revise labeling "to include a warning about a clinically significant hazard." 21 C.F.R. § 201.57(c)(6)(i). Perhaps for this reason, Shire cites no case holding

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[2] https://www.fda.gov/files/drugs/published/Labeling-for-Human-Prescription-Drug-and-Biological-Products---Implementing-the-PLR-Content-and-Format-Requirements.pdf.

that the Highlights regulations bar CBE changes to other portions of the labeling.[3]

Further contradicting Shire's view, Mr. Blackburn's reply brief pointed out that FDA regulations and guidance directly address the effect of CBE changes on the content of the Highlights section. *See* Appellant's Reply 23 (citing 21 C.F.R. § 201.57(a)(5) (requiring Highlights to include a list of the sections that contain substantive changes, including CBE changes to Warnings and Precautions), and FDA, *Guidance for Industry: Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* at 8 ("When substantive labeling changes have been made to any

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[3] Shire cites two unreported district court cases for the point that manufacturers cannot alter the Highlights without FDA approval. Pet. 25. In *Brashear v. Pacira Pharmaceuticals, Inc.*, 2023 WL 3075403, at *4 (S.D. Ohio Apr. 25, 2023), the court first held that changes to Warnings require changes to Highlights, but then considered whether "the availability of the CBE process" would "change this result." Concluding that it did not, the court explained that because the plaintiff had "not identified any newly acquired safety information that would have allowed [the manufacturer] to initiate the CBE process, [the manufacturer] could not have changed [the drug's] warning label without first getting FDA approval." *Id.* at *5. In contrast here, the Eleventh Circuit held that Mr. Blackburn had met the evidentiary standard, at least at the summary judgment phase. Pet. App. 5 (finding that Shire's contention "that it could not have supported a label change with newly acquired information, or, at the least, [that] Blackburn failed to identify any … is belied by the record"). In the second unreported district court case cited by Shire, *Patton v. Forest Laboratories, Inc.*, 2018 WL 5269239, at *11 (C.D. Cal. Sept. 19, 2018), the plaintiffs agreed with the defendants that changes to Highlights require FDA approval, and the court's brief discussion does not suggest that FDA regulations prohibit changes to the Warnings in the Full Prescribing Information.

of the following sections [including Warnings and Precautions] of the [Full Prescribing Information] within the preceding 12 months, the heading(s) of the changed section(s) must be listed in Highlights under the heading Recent Major Changes.")).

Moreover, Mr. Blackburn's reply brief noted that, where a revision to the Full Prescribing Information to enhance safety counsels in favor of a change to the Highlights, the FDA "typically waives" prior approval for changes to the Highlights section. Appellant's Reply 24 (quoting 78 Fed. Reg. 67985, 67993 (Nov. 13, 2013)). Finally, the reply brief pointed out that, because the Highlights section regulations did not apply to Lialda for several years after it entered the market, Shire's argument concerning Highlights would not support its preemption argument, even if it were not otherwise non-meritorious. *Id*.

Read in light of the claim alleged, Shire's argument to the Eleventh Circuit, and Mr. Blackburn's reply, Shire's misreading of the last paragraph of the opinion below is clear: The court did not hold that the CBE process can be used to revise the Highlights section. It held that the existence of the Highlights section does not bar CBE revisions to Warnings and Precautions in the Full Prescribing Information. The holding follows from the regulatory scheme and is consistent with the relevant case law of this Court and the courts of appeals. Conversely, no appellate decision agrees with Shire that the requirements of the Highlights section bar CBE changes to the Warnings.

II. Review of the non-precedential decision in this non-final case is unwarranted.

Shire's mischaracterization of the claim at issue and the decision below relates to an additional reason

why this case does not warrant review: The petition challenges an interlocutory decision under a summary judgment standard, where facts remain in dispute. As the court of appeals stated, "[o]ur review is circumscribed by the standard for summary judgment," Pet. App. 6, and "[o]n this summary judgment record, we cannot say that federal law preempts Blackburn's state-law cause of action," *id.* 8.

Although this Court has jurisdiction to review interlocutory decisions of federal courts of appeals under 28 U.S.C. § 1254(1), "[o]rdinarily, in the certiorari context, th[e] [C]ourt should not issue a writ of certiorari to review a decree of the circuit court of appeals on appeal from an interlocutory order, unless it is necessary to prevent extraordinary inconvenience and embarrassment in the conduct of the cause." Stephen Shapiro, Kenneth Geller, et al., *Supreme Court Practice* § 4.18, at 4-55 (11th ed. 2019) (citation and internal quotation marks omitted). The Court "generally await[s] final judgment in the lower courts before exercising [its] certiorari jurisdiction." *Virginia Military Inst. v. United States*, 508 U.S. 946, 946 (1993) (Scalia, J., concurring in the denial of certiorari).

The posture of this case is far from "extraordinary." Mr. Blackburn is pursuing a garden-variety state-law tort suit. Factual disputes remain, and the trier of fact may decide in favor of either party. If Shire prevails, review on the question presented in the petition would not be necessary (or appropriate). If Mr. Blackburn prevails, it will be clear at that time whether his claim turned on Shire's failure to make changes that FDA regulations bar, as Shire argues here, or whether his claim resembles those in *Wyeth* and other cases, where the manufacturer's failure-to-warn could have been

cured through changes to the Full Prescribing Information through the CBE process.

CONCLUSION

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

Respectfully submitted,

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