No. 24-977

IN THE

Supreme Court of the United States

MERCK SHARP & DOHME CORPORATION,
Petitioners,

v.

DORIS ALBRECHT, ET AL.,
Respondent.

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

BRIEF FOR THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AS *AMICUS CURIAE* IN SUPPORT OF CERTIORARI

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INTERESTS OF *AMICUS CURIAE*[1]

The Pharmaceutical Research and Manufacturers of America ("PhRMA") represents the country's leading innovative biopharmaceutical companies, which are laser-focused on developing innovative medicines that transform lives and create a healthier world. Together, PhRMA is fighting for solutions to ensure patients can access and afford medicines that prevent, treat and cure disease. Over the last decade, PhRMA member companies have invested more than $800 billion in the search for new treatments and cures, and they support nearly 5 million jobs in the United States. *See* PhRMA, *2024 PhRMA Annual Membership Survey* 3 (2024), https://perma.cc/6NB6-3F6V.

This case presents a question of significant importance for PhRMA's members: whether after this Court's 2019 decision in *Merck v. Albrecht*, pharmaceutical manufacturers can face state tort-law liability for failing to include warning language on their labeling after the Food and Drug Administration ("FDA") has determined that such a warning is not medically justified. The burdens of product liability

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[1] Pursuant to Rule 37.6, *amicus* affirms that no counsel for a party authored this brief in whole or in part and that no person other than *amicus*, its members, or its counsel made any monetary contributions intended to fund the preparation or submission of this brief. A list of PhRMA members is available at http://www.phrma.org/about#members. Merck & Co. is a member of PhRMA, but did not contribute financially to the preparation of this brief. The parties were timely notified of *amicus*'s intent to file this brief.

litigation are already substantial for life sciences companies, and a regime that permits these companies to be held liable for failing to do what the FDA has determined is not medically appropriate would disrupt regulation, hamper innovation, and harm patient health. The Court should grant certiorari and reverse the Third Circuit's judgment.

INTRODUCTION AND SUMMARY OF ARGUMENT

Nearly six years ago in *Merck Sharp & Dohme v. Albrecht*, this Court resolved widespread confusion on how to apply the "clear evidence" standard to determine whether the FDA would have approved a change to a medication's labeling, thus preempting a state-law failure to warn claim. 587 U.S. 299 (2019). In *Albrecht*, the Third Circuit had held that a jury should decide the preemption question, and that a jury would have to find "clear and convincing evidence" that the proposed warning was preempted. *In re Fosamax (Alendronate Sodium) Prod. Liab. Litig.*, 852 F.3d 268, 286 (3d Cir. 2017) ("*Fosamax I*"). This Court firmly rejected that approach, and instead laid out a test for courts to address the preemption question. *Albrecht*, 587 U.S. at 303.

Now, history repeats. The Third Circuit once again veers sharply away from its sister circuits. In this case, a continuation of the Fosamax litigation against Merck, the Third Circuit found that a "heavy *Albrecht* presumption" against preemption is determinative in cases where there is any ambiguity in the FDA's official response to a potential labeling change. This stark holding is at war with both the text of *Albrecht* and how other lower courts have applied that decision. By loading the dice with an effectively dispositive presumption and by paying little attention to surrounding factual and statutory context, the Third Circuit once again places itself as an extreme outlier. Without intervention by this Court, what had become a reasonably settled regime will be reshuffled and

cause mischief and chaos once again in the lower courts.

In reaching its decision, the Third Circuit does not contend with the realities of the pharmaceutical industry and the FDA's obligations under the Food and Drug Administration Amendments Act ("FDAAA"). In taking a highly constrained view of FDA's statutorily mandated decision making, the decision below incentivizes companies to inundate the FDA with repeated submissions of every linguistic variation of a label in hopes of heading off an argument in some future litigation that the FDA's "No" didn't really mean "No." This Court in *Albrecht* rejected such a nonsensical regime; it directed district courts to evaluate the regulatory record and make its best factual determination, unencumbered by any case-steering presumption. That is exactly what the district court did here. The Third Circuit's reversal of that factual determination is not so much a critique of the district judge's performance of that duty as much as it is a denunciation of this Court's mandate in *Albrecht*.

Such an outcome is highly detrimental to patient safety, especially when the FDA is already statutorily obligated under the FDAAA to mandate new labeling if it identifies a new safety risk. The Third Circuit's presumptively-never preemption standard risks exposing manufacturers to unfair liability for health outcomes the FDA has determined cannot be linked to the medicine, which in turn will materially diminish innovation and impact public health.

ARGUMENT

I. THE THIRD CIRCUIT'S DECISION DIVERGES FROM SIX YEARS OF POST-*ALBRECHT* CASE LAW, CREATING A CIRCUIT SPLIT THAT DEMANDS RESOLUTION.

A. In *Albrecht*, the Supreme Court Resolved a Longstanding Split on Preemption.

The Supreme Court in *Albrecht* provided guidance to resolve confusion in how lower courts were applying the preemption analysis set forth in *Wyeth v. Levine*, 555 U.S. 555 (2009). In *Wyeth*, the Court laid out the "clear evidence" test to assess whether the FDA would have approved a change to a medication's labeling, and in that case found the FDA had never given "more than passing attention" to the warning plaintiffs sought. *Wyeth*, 555 U.S. at 571–72. Without guidance about the type and quantum of evidence required to meet this burden, lower courts varied in their interpretation of the "clear evidence" test in practice. *See, e.g.*, *Fosamax I*, 852 F.3d at 282 (the clear evidence standard is "cryptic and open-ended, and lower courts have struggled to make it readily administrable"); *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 391 (7th Cir. 2010) (the Court "did not clarify what constitutes 'clear evidence.' Therefore, the only thing we know for sure is that the evidence presented in *Levine* did not meet this exacting standard.").

In *Merck Sharp & Dohme Corp. v. Albrecht*, 587 U.S. 299 (2019), this Court provided direction on how

to apply *Wyeth*'s clear evidence test. First, this Court overturned the Third Circuit's holding that the question of whether the FDA had rejected a warning was one for the jury, instead stating that this was a legal issue to be decided by the judge. *Albrecht*, 587 U.S. at 310. Second, and more crucially, this Court rejected the notion that *Wyeth*'s clear evidence test was some kind of heightened evidentiary standard, and instead held that "the judge must simply ask himself or herself whether the relevant federal and state laws irreconcilably conflict." *Id.* at 315 (cleaned up). Finally, the Court in *Albrecht* provided a two-part test for preemption which required evidence (1) "that the drug manufacturer fully informed the FDA of the justifications for the warning," and (2) that, in turn, an action taken by the FDA "informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Id.* at 303.

Since *Albrecht*, lower courts have applied its preemption framework to contexts where the FDA indicated that a proposed additional warning—whether specifically considered at the time by FDA or proposed by some lawyer in some future litigation—would not have been approved.

B. The Third Circuit's Disregard of *Albrecht* Disturbs Six Years of Consistent Application.

The lower courts have been routinely applying *Albrecht* in a manner consistent with the two-part test, without layering on substantive canons against preemption. Subsequent cases further refined the analysis to track both the language of *Albrecht* and

the Changes Being Effected ("CBE") regulation that *Wyeth* explained provided the narrow pathway to avoid preemption. *See* 21 C.F.R. § 314.70(c)(6)(iii)(A). That test, since adopted by courts across the nation, asks (1) is there "newly acquired information" such that the CBE regulatory pathway can be invoked, and if so, (2) whether there is "clear evidence" under *Albrecht* that the FDA would have rejected such a CBE application. *See, e.g.*, *In re Zofran (Ondansetron) Prods. Liab. Litig.*, 57 F.4th 327, 336 (1st Cir. 2023); *Knight v. Boehringer Ingelheim Pharms., Inc.*, 984 F.3d 329, 338–39 (4th Cir. 2021); *In re Incretin-Based Therapies Prod. Liab. Litig.*, 524 F. Supp. 3d 1007, 1017 (S.D. Cal. 2021), *aff'd on other grounds*, No. 21-55342, 2022 WL 898595 (9th Cir. Mar. 28, 2022); *Hickey v. Hospira Inc.*, 102 F.4th 748, 754 (5th Cir. 2024) (per curiam).[2]

In postulating an effectively dispositive "strong presumption" against preemption, while at the same time simply casting aside the district court's factual determinations as to the regulatory record of the FDA's decision, the Third Circuit has become an outlier in its application of *Albrecht*. *See* Pet. App. 62a. (holding that the "strong presumption [against preemption] that the Supreme Court has established will likely be determinative."). Rather than place any weight on the surrounding factual context or regulatory history or defer to the district court's meticulous

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[2] *See also Lyons v. Boehringer Ingelheim Pharms., Inc.*, 491 F. Supp. 3d 1350, 1363 (N.D. Ga. 2020); *Mahnke v. Bayer Corp.*, 2019 WL 8621437, at *3 (C.D. Cal. Dec. 10, 2019); *Bueno v. Merck & Co.*, 746 F. Supp. 3d 853, 875 (S.D. Cal. 2024); *Ridings v. Maurice*, 444 F. Supp. 3d 973, 991 (W.D. Mo. 2020).

evaluation of that record, the Third Circuit effectively held that any ambiguities in the regulatory record—here, FDA's Complete Response Letter ("CRL")[3]—"are swept away by the heavy *Albrecht* presumption." *Id.* at 66a.

First, the Third Circuit's reasoning is irreconcilable with *Albrecht*, which doesn't mention any presumptions and explicitly held that district judges are best equipped "to understand and to interpret agency decisions in light of the governing statutory and regulatory context." *Albrecht*, 587 U.S. at 315–16. *Albrecht* does not apply a presumption against preemption, and instead directs judges to "simply ask … whether the federal and state laws irreconcilably conflict." *Id.* at 315 (cleaned up) (also noting that a "hypothetical or potential conflict is insufficient"). The Third Circuit instead contorts *Albrecht* by latching on to stray references to words like "difficult" and "demanding" to create a "strong presumption," even though this Court never even used the word "presumption" in its *Albrecht* majority opinion. Pet. App. 62a. To the extent that any consideration of a presumption against preemption is necessary, *Wyeth's*

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[3] A CRL is issued by the FDA in denying a labeling proposal, and "describes[s] all of the specific deficiencies that the agency has identified" and "when possible ... recommend[s] actions that the applicant might take to place the application or abbreviated application in condition for approval." 21 C.F.R. § 314.110(a). The CRL "reflects FDA's complete review of the data submitted." *Id.* § 314.110(a)(2). After receiving a CRL, manufacturers have the option to resubmit the application addressing all the deficiencies, withdraw the application without prejudice to a subsequent submission, or ask the agency for a hearing. *Id.* § 314.110(b).

"clear evidence" test itself already bakes in that notion. *Wyeth*, 555 U.S. at 565, 575. The irregularity of this decision is only confirmed by the fact that no other lower courts have applied *Albrecht* in this way.

Second, the Third Circuit's deviation creates significant confusion on the application of *Albrecht* and undoes the clarity this Court attempted to instill with that decision. Other post-*Albrecht* cases do not invoke a presumption against preemption in evaluating (1) whether new information was acquired that would permit a manufacturer to make a labeling change using the CBE process, and (2) whether the FDA would have rejected such a labeling change. In *Cerveny v. Aventis*, the Tenth Circuit rejected an argument to narrowly read *Albrecht* as only applying to situations where the drug manufacturer itself sought labeling changes, and instead found preemption where the FDA rejected a citizen petition seeking to provide a warning for the health outcome at issue. 783 F. App'x 804, 808 n.9 (10th Cir. 2019). In affirming its prior decision, the Tenth Circuit did not rely on any substantive presumptions which could skew the inquiry against preemption. *Id.*

In *Dolin v. GlaxoSmithKline LLC*, the Seventh Circuit applied *Albrecht* without a presumption against preemption and affirmed a district court finding that the FDA had rejected a drug-specific warning by mandating uniform class-wide labels. 951 F.3d 882, 891 (7th Cir. 2020). Similarly in *In re Zofran (Ondansetron) Prods. Liab. Litig.*, the First Circuit affirmed the district court's preemption finding where FDA had possession of the latest studies and approved a label without the warning plaintiffs sought. 57

F.4th at 342. The First Circuit did not apply any presumptions or note the "difficulty" entailed in establishing preemption and instead simply held that the "FDA in approving the label stating 'not-X' necessarily rejected plaintiffs' prominently presented case for stating 'X'." *Id.* Notably, the First Circuit did not require an express rejection of a proposed warning but instead found an implied rejection based on the FDA's approval of a contrary label. *Id.*

Even more courts have both declined to apply a presumption against preemption and also made ample use of extrinsic factual context when applying *Albrecht* to determine whether manufacturers lacked the newly acquired information necessary to invoke the CBE process. *See, e.g.*, *Mahnke*, 2019 WL 8621437, at *4 (examining universe of scientific literature in finding no newly acquired information); *In re Incretin-Based Therapies*, 524 F. Supp. 3d at 1029–33 (holding that manufacturer did not have newly acquired information and there was clear evidence FDA would not have approved CBE based in part on review of extrinsic evidence); *In re Zofran (Ondansetron)*, 57. F4th at 26 (analyzing scientific studies to determine manufacturer did not have newly acquired information); *Bueno*, 746 F. Supp. 3d at 877–80 (reviewing state of scientific analysis in finding no newly acquired information and preemption); *Warner v. Amgen Inc.*, 2025 WL 490720, at *9–10 (D. Mass. Feb. 13, 2025) (reviewing published articles in finding no newly acquired information); *Hickey*, 102 F.4th at 757–59 (analyzing pre-approval and post-approval scientific literature in finding no newly acquired information).

By overlaying its dispositive "*Albrecht* presumption" and disregarding the relative weight of statutory and factual context, the Third Circuit has created confusion and a significant circuit split. PhRMA members do not have the luxury of treating *Fosamax II* as an aberration, both because it creates a higher bar for preemption fundamentally inconsistent with this Court's decision in *Albrecht* and because a substantial number of PhRMA members are headquartered in the Third Circuit. Absent intervention and review by this Court, the standard created by *Albrecht* will evaporate in the face of drastically different presumptions and applications of the two-part test.

II. THE *FOSAMAX II* DECISION DISREGARDS FDA'S LABELING OBLIGATIONS AND THREATENS ITS EFFECTIVENESS.

The Third Circuit's decision pays insufficient weight to the FDA's extensive labeling oversight and corresponding statutory obligations under the FDAAA. Instead of recognizing that the FDA is obligated to work with manufacturers to update warning labels in light of new scientific evidence, the *Fosamax II* decision encourages the submission of seriatim iterations of labeling language to try to anticipate and head off how some creative plaintiff's lawyer down the road might second-guess the regulatory record. That result risks straining the FDA's review capabilities and will ultimately impact public health.

A. The Third Circuit's Ruling Threatens to Overwhelm the FDA's Review Capabilities.

The FDA must strike a delicate balance in effectuating proper pharmaceutical labeling. Labeling must impart critical information regarding safety and the effective use of a medicine, while also communicating this content in a manner that is helpful to healthcare professionals. The FDA must be wary of including warnings that are not supported by science, because such "overwarning" carries serious risks for patients. First, physicians may disregard lengthy labels full of speculative warnings, and overlook important, scientifically validated safety information. *See Albrecht*, 587 U.S., at 304 ("the hierarchy of label information is designed to prevent overwarning so that less important information does not overshadow more important information") (quotation marks omitted). Second, warnings that are not grounded in science discourage the beneficial usage of medicines for patients who need it. *See id.* (Label information is "designed to exclude exaggeration of risk, or inclusion of speculative or hypothetical risks, that could discourage appropriate use of a beneficial drug" (cleaned up)). All medicines have risks, and the prescribing medical professional must weigh those risks against a medicine's potential benefit for a patient. Distorting this balance by either overstating *or* understating the risks inhibits medical professionals and in turn threatens the wellbeing of patients.

The Third Circuit's preemption ruling will distort the incentives and lead manufacturers to submit multiple iterations of labeling supplements to protect

against state-law claims from enterprising plaintiff's lawyers. In *Buckman v. Plaintiffs' Legal Committee*, this Court recognized that state law "fraud-on-the-FDA" claims were preempted because they would incentivize drug manufacturers to "submit a deluge of information that the [FDA] neither wants nor needs" out of "fear that their disclosures … will later be judged insufficient in state court." 531 U.S. 341, 351 (2001). The Third Circuit's decision here will create precisely the same incentives because of its narrow reading of FDA's response.

In the decision below, the Third Circuit rejected the district court's factual finding and instead concluded that the FDA's CRL rejection letter was ambiguous because it was possible that the FDA rejected Merck's proposed warning based on a semantic disagreement over the term "stress fractures." Pet. App. 61a–62a. The Third Circuit went so far as to admonish the district court for not reading the CRL "in a manner that disfavors pre-emption." *Id.* at 66a. In other words, according to the Third Circuit, the district court erred not in its factual answer to the factual question per se, but rather because it didn't rig the factual question in the first place.

In the same vein, the Third Circuit found fault in the district court's consideration of certain evidence in the regulatory record—like a subsequent FDA phone call and the FDA's amicus brief which showed the FDA did not believe there was sufficient evidence to support a warning—because in its view "extrinsic evidence … cannot be determinative in a case like this." *Id.* at 66a–67a. The myopic refusal to permit consideration of *any* extrinsic evidence to interpret FDA's

actions cannot be reconciled with this Court's directive in *Albrecht*, which charges the district court as factfinder to parse the regulatory record "to understand and to interpret agency decisions in light of the governing statutory and regulatory context." *Albrecht*, 587 U.S. at 315–16. Assessing the regulatory record can be a complicated task—one reason this Court rejected the Third Circuit's original peculiar notion that a jury should sort this out—yet the Third Circuit's revised approach here would yield a similar result: unless there is zero ambiguity in the regulatory record, a district court's factual finding of clear evidence must be reversed. But rarely will the regulatory record be bereft of some ambiguity that an interested advocate after the fact could try to leverage. *See, e.g.*, *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 814 (7th Cir. 2018) (plaintiffs arguing that FDA labeling rejection was based on the placement location and not the content); *Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1101–02 (10th Cir. 2017) (plaintiffs arguing that FDA labeling rejection was not dispositive because it was submitted by a citizen instead of a manufacturer).

After all, CRLs are drafted by scientists, not lawyers versed in the nuances of preemption doctrine. The scientists who draft these non-public letters are not writing for courts, but to parties who have been

engaged in a back-and-forth dialogue with the FDA.[4] A CRL reflects FDA's complete review of the submitted data and must be read in context with FDA's broader statutory obligations. *See* Br. for the United States as Amicus Curiae Supporting Pet'r at 32, *Merck Sharpe & Dohme Corp. v. Albrecht*, 587 U.S. 299 (2019) (No. 17-290) ("[I]f FDA determines that a safety-based labeling change is warranted based on the data, FDA will attempt promptly to identify easily correctible deficiencies in the proposed text and will develop final labeling text with the manufacturer in an iterative process.").

For fear that any tinge of doubt would render an FDA decision ambiguous, manufacturers will be incentivized to continually go back to the FDA and ask again and again—"Are you sure?" "What about these words?" This dynamic will extend regulatory interactions, increase meeting requests, delay implementation of labeling changes, and multiply submissions of labeling supplements that by law FDA must devote resources to consider and respond to. *See* 21 C.F.R. § 314.70(b)(2)(v) (Prior Approval Supplement submissions); 21 C.F.R. § 314.70(c)(6)(iii)(A) (CBE supplement submissions to reflect "newly acquired information"); *see also* Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922,

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[4] *See* Mark Senak, *Potayto—Potahto? The Meaning of the FDA's "Complete Response" Letters*, 1(7) Am. Health Drug Benefits 30–31 (2008), https://pmc.ncbi.nlm.nih.gov/articles/PMC4106573 ("[T]he contents of a … complete response letter are considered proprietary, and the FDA does not divulge the contents of such letters, nor does it issue a press release.").

3934 (Jan. 24, 2006) ("FDA reviews all [CBE] submissions…."). Eliciting endless "yes, we really meant it" responses from FDA serves no public health purpose.

Indeed, diverting the FDA's attention towards such iterative submissions carries significant risks. *See Lofton v. McNeil Consumer & Specialty Pharm.*, 672 F.3d 372, 380 (5th Cir. 2012) (When manufacturers are compelled "to flood the FDA with information …. [the FDA] loses control over its ability, based on scientific expertise, to prescribe—and intelligently limit—the scope of disclosures necessary for its work."). The corresponding results of overwarning or failing to include scientifically legitimate warnings on medication labeling presents a serious threat to patient wellbeing.

B. The FDA's Obligations Under the FDAAA Already Ensure That Labeling Is Accurate.

The FDA's existing statutory obligations as set forth in the FDAAA ensure that the kind of labeling rejection in this case could not have been due to some linguistic quibble. In addition to reviewing specific labeling changes that manufacturers propose, the FDA independently has the statutory obligation to consider

whether labeling remains adequate in light of the existing scientific record.[5] Under the FDAAA, once the FDA "becomes aware of … new safety information … that [it] determines should be included in the labeling of the drug," the FDA must promptly engage with the manufacturer to amend the drug's labeling. 21 U.S.C. § 355(o)(4)(A). If the FDA disagrees with the manufacturer's response or other proposed changes, it cannot stand idly by. Per § 355(o)(4)(C), the FDA "shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety … information, and if so, the contents of such labeling changes." In addition, under § 355(o)(4)(E) the FDA is empowered to "issue an order directing the [manufacturer] to make such a labeling change as the [FDA] deems appropriate to address the new safety … information."

Taken together, the changes enacted by the FDAAA obligate the FDA to effect warning labeling changes if justified by the scientific evidence, irrespective of where it learns of the information and whether a company has proposed a labeling change. If the FDA were rejecting the labeling change based on a dispute over word selection or because it needed more information from the manufacturer, § 355(o)(4) requires immediate action or follow-up. *See Albrecht*, 587 U.S.

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[5] Manufacturers are required to report "serious and unexpected" adverse events to the FDA within 15 days of receipt and to periodically report all other adverse events. 21 C.F.R. § 314.80. The FDA also receives adverse event reports through a voluntary reporting system, MedWatch. *MedWatch: The FDA Safety Information and Adverse Event Reporting Program*, FDA, https://www.fda.gov/Safety/MedWatch/default.htm.

at 324 (Alito, J., concurring) (Finding that because of § 355(o)(4) "if the FDA declines to require a label change despite having received considered information regarding a new risk, the logical conclusion is that the FDA determined that a label change was unjustified."). Such a conclusion is supported by the "presumption of regularity" which holds that the FDA acted in accordance with its statutory obligations. *Id.*

Instead of giving sufficient weight to the significant obligations imposed by § 355(o)(4) and the finding that the statute was "highly relevant to the pre-emption analysis," *id.* at 325, the Third Circuit gives it only passing consideration. The court turns to § 355(o)(4) only after it has already enshrined its "heavy *Albrecht* presumption" against preemption that renders the slightest ambiguity dispositive. Pet. App. 66a. The Third Circuit's side-stepping of Justice Alito's admonition only underscores the absurdity of using a presumption against preemption in assessing FDA actions. The cases that the Third Circuit cites applying the presumption against preemption concern the interpretation of statutes or regulations, rooted in the idea that Congress generally does not intend to displace traditional areas of state regulation. *See, e.g.*, *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005); *Wyeth*, 555 U.S. at 575. Here, the FDA declines to amend labeling in the absence of sufficient evidence all the time and indeed has a statutory obligation to do so. There is no reason for the Third Circuit to have presumed that the FDA did *not* act consistent with the FDAAA's statutory imperative.

In justifying its disregard of the FDAAA, the Third Circuit looked "beyond the letter" to examine extrinsic

evidence which purportedly showed that the FDA was still considering the science on atypical femoral fractures. Pet. App. at 71a. The court found that the FDA "had not formalized a decision" and was entitled to "take its time." *Id.* at 73a–74a. This conclusion is seemingly in conflict with Justice Alito's own takeaway from the factual evidence. *See Albrecht*, 587 U.S. at 328 (Alito, J., concurring) ("for years the FDA was: aware of this issue, communicating with drug manufacturers, studying all relevant information, and instructing healthcare professionals and patients alike to continue to use Fosamax as directed."). In addition, the Third Circuit's resort to extrinsic evidence is inconsistent with its rejection of the district court's consideration of extrinsic evidence to conclude that the FDA's CRL foreclosed the label change. More fundamentally, if indeed the FDA was so uncertain, then it would have been obligated to reject the sort of warning label Plaintiffs demand in this case. While the FDA is considering what to do and evaluating the relevant scientific evidence, manufacturers are forbidden from striking out on their own and changing their labeling. *See* 21 C.F.R. § 314.110(b) (listing available applicant actions after receiving a CRL as resubmission, withdrawal, or request for a hearing). The Third Circuit thus contorted the factual record, the regulatory framework, and the evidentiary standard to find that somehow the manufacturer was still permitted to make a label change notwithstanding the FDA's rejection of that change in a CRL.

III. THE THIRD CIRCUIT'S RULING HAMPERS MANUFACTURER INNOVATION AND HARMS PATIENT HEALTH.

The Third Circuit's decision fundamentally undermines the rational preemption framework this Court set forth in *Albrecht*. The fact that a large number of PhRMA's members are located within the Third Circuit makes this decision all the more troubling because of the impact it will have on patient health and innovation.

Bringing a new medicine to market is a lengthy and expensive process. *See Mutual Pharm. Co., Inc. v. Bartlett*, 570 U.S. 472, 476 (2013) ("The process of submitting an NDA is both onerous and lengthy."); *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 612 (2011) ("[A] manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate. Meeting those requirements involves costly and lengthy clinical testing." (citations omitted)). On average, developing a new medicine and obtaining FDA approval takes ten to fifteen years and costs $2.6 billion.[6] PhRMA member companies invest more than 22% of their total annual domestic sales on research and development—an estimated $71.3 billion in

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[6] PhRMA, *Biopharmaceuticals in Perspective: Fall 2020*, at 27 (2020), https://perma.cc/VD85-GA8E; *see also* Joseph A. DiMasi et al., *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. Health Econ. 20 (2016).

2023.[7] The drug development process involves several steps including laboratory and animal studies, an Investigational New Drug application ("IND"), three phases of human clinical trials, and finally a New Drug Application ("NDA") which can exceed 100,000 pages in length.[8] The research efforts also involve significant risks, with a 90% failure rate for drugs that enter clinical trials, let alone the many more preclinical candidates which fail earlier in the process.[9]

All of these efforts are geared towards getting the science right: first, confirming the company and the FDA understand the risk-benefit profile for a prospective medicine and determining that its benefits outweigh its risks; second, ensuring that the labeling accurately reflects those risks and benefits so physicians working with their patients can make the proper decision whether the medicine is right for that patient. It is unfair and intolerable for a company to face massive litigation exposure for claims that the medicine's labeling should have included a warning that the FDA has rejected. The current federal court docket is loaded with tens of thousands of lawsuits

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[7] PhRMA, *2024 PhRMA Annual Membership Survey* 4 tbl. 2 (2024), https://perma.cc/6NB6-3F6V.

[8] PhRMA, *Biopharmaceutical Research & Development: The Process Behind New Medicines* 14 (2015), https://perma.cc/P237-5EVM.

[9] Duxin Sun et al., *Why 90% of Clinical Drug Development Fails and How to Improve It*, 12(7) Acta Pharm. Sinica B. 3049–62 (2021), https://pubmed.ncbi.nlm.nih.gov/35865092/.

against pharmaceutical manufacturers.[10] Today, out of sixty-seven pending product liability multidistrict litigation proceedings, eighteen involve pharmaceuticals. *See* U.S. Jud. Panel on Multidist. Litig., *MDL Statistics Report: Docket Type Summary* (Apr. 1, 2025), https://perma.cc/7LRS-9FWV.

This litigation risk bears heavily on a pharmaceutical company's decision to invest in further innovation. *See* Daniel E. Troy, *The Case for FDA Preemption*, *in Federal Preemption: States' Powers, National Interests* 87 (2007) ("Massive tort verdicts can dramatically skew the cost side of [the] equation ... pharmaceutical manufacturers may take overly risk-averse positions with respect to drugs that, despite their unquestioned benefits, do not have the potential to produce large revenue streams."). Permitting an "overly aggressive tort environment" can lead to "increased costs and risks of doing business in an area," "disincentives for innovations which promote consumer welfare," and "deterrence of economic development and job creation incentives. Perryman Grp., *Economic Benefits of Tort Reform* 4 (Nov. 4, 2019), https://perma.cc/CMA6-XYMJ.

Both before and in the wake of *Albrecht*, courts applying a rational preemption framework as required by *Albrecht* have tempered this trend and have ended major litigations when the court has determined that the warning sought by plaintiffs was not justified.

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[10] *See* Admin. Office of the U.S. Courts, *Table C-2A: U.S. District Courts-Civil Cases Commences, by Nature of Suit, During the 12-Month Periods Ending September 30, 2020 through 2024* (2024), https://perma.cc/4HQG-CXYC.

See, e.g., *Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 709 (2d Cir. 2019) (ending Eliquis litigation); *In re Zofran (Ondansetron)*, 57 F.4th at 343 (ending Zofran litigation); *Knight*, 984 F.3d at 341 (finding Pradaxa claims preempted); *Adkins v. Boehringer Ingelheim Pharms., Inc.*, 2020 WL 1890681 (Conn. Super. Ct. Mar. 13, 2020) (finding Pradaxa warning claims preempted in consolidated state court proceeding); *In re Incretin-Based Therapies*, 524 F. Supp. 3d at 1051 (ending incretin-based therapies MDL).

The Third Circuit's approach—and its effectively case-dispositive presumption against preemption—is a significant outlier. Holding manufacturers liable for failing to include warning language based on a heavy presumption against preemption and a narrow reading of FDA action would ultimately shift resources away from innovation to instead pay for expensive litigation defense. The result of the Third Circuit's preemption framework is that juries will be left to scrutinize whether a company should have altered their labeling in the face of contrary guidance from the FDA. That is precisely the opposite of the result this Court intended in *Albrecht*, where it found lay jurors are ill-equipped to make the sort of nuanced, complex risk-benefit calculations that animate the FDA's review of label change applications. *See Albrecht*, 587 U.S. at 316 ("The complexity of the preceding discussion of the law helps to illustrate why we answer this question by concluding that the question is a legal one for the judge, not a jury"); *see also Riegel v. Medtronic, Inc.*, 552 U.S. 312, 325 (2008) (whereas "the experts at the FDA" apply a "cost-benefit analysis," a jury "sees only the cost of a more dangerous design, and is not

concerned with its benefits; the patients who reaped those benefits are not represented in court"). By overlaying additional hurdles on top of *Albrecht* and discounting the relevance of factual and statutory context, the Third Circuit's decision risks undermining innovation and patient wellbeing.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

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