No. ____

IN THE

Supreme Court of the United States

MERCK SHARP & DOHME CORPORATION,

Petitioner,

v.

DORIS ALBRECHT, ET AL.,

Respondents.

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

PETITION FOR WRIT OF CERTIORARI

STEPHEN E. MARSHALL
VENABLE LLP
750 East Pratt St.
Baltimore, MD 21202

NOEL J. FRANCISCO
Counsel of Record
JEFFREY R. JOHNSON
JOHN HENRY THOMPSON
JONES DAY
51 Louisiana Ave., NW
Washington, DC 20001
(202) 879-3939
nfrancisco@jonesday.com

JOHN R. BOULÉ III
JONES DAY
555 South Flower St.
Fiftieth Floor
Los Angeles, CA 90071

Counsel for Petitioner

QUESTION PRESENTED

Six years ago, this Court unanimously vacated the Third Circuit's ruling imposing a heightened standard for preemption, and remanded to apply a two-part test asking if (i) "the drug manufacturer fully informed the FDA of the justifications for the warning required by state law," and (ii) "the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Merck Sharp & Dohme Corp. v. Albrecht*, 587 U.S. 299, 303 (2019). On remand, the district court found both parts of the test satisfied. But the Third Circuit again rejected preemption, this time by adopting a "heavy" evidentiary presumption under which the record must be read "in a manner that disfavors pre-emption," thus foreclosing a court's consideration of extrinsic evidence (such as the FDA's contemporaneous statements and even its later representations in court), and allowing preemption only if the FDA's action is "abundantly clear" on its face. Pet.App.66a.

The question presented thus remains:

If a pharmaceutical manufacturer fully informs the FDA of all material information bearing on a drug's potential risk and seeks approval to warn of that risk on the label (as the district court and Court of Appeals both found), but the FDA formally denies the request without mandating any alternative warning, may the manufacturer nonetheless be held liable under state law for failure to warn of that risk?

PARTIES TO THE PROCEEDING AND RULE 29.6 STATEMENT

Petitioner is Merck Sharp & Dohme Corporation (Merck), which is a wholly owned subsidiary of Merck & Co., Inc. No publicly held corporation owns 10% or more of the stock of Merck & Co., Inc.

Respondents—identified by name and Third Circuit docket number in Appendix E (Pet.App.213a-270a)—are more than 1000 plaintiffs who brought state-law failure-to-warn claims against Merck that were consolidated in a multi-district litigation in the District of New Jersey. The Third Circuit resolved their appeals in one consolidated opinion. Pet.App.1a-76a. Pursuant to this Court's Rule 12.4, Merck files this consolidated petition to review that decision.

STATEMENT OF RELATED PROCEEDINGS

This case arises from the following proceedings:

- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, Nos. 11-cv-5304, 08-cv-08 (D.N.J. June 27, 2013) (reported at 951 F. Supp. 2d 695)
- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, No. 08-cv-08 (D.N.J. Mar. 26, 2014) (reported at 2014 WL 1266994)
- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, Nos. 12-cv-1492, 08-cv-08 (D.N.J. June 17, 2014) (reported at 2014 WL 2738224)
- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, Nos. 14-1900 et al. (3d Cir. Mar. 22, 2017) (reported at 852 F.3d 268)
- *Merck, Sharp & Dohme Corp. v. Albrecht*, No. 17-290 (May 20, 2019) (reported at 587 U.S. 299)
- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, MDL No. 2243, No. 08-cv-08 (D.N.J. Mar. 23, 2022) (reported at 593 F. Supp. 3d 96)
- *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, No. 22-3412 (3d Cir. Sept. 20, 2024) (reported at 118 F.4th 322)

There are no other proceedings in state or federal trial or appellate courts, or in this Court, directly related to this case within the meaning of this Court's Rule 14.1(b)(iii).

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INTRODUCTION

Merck told the FDA that its drug Fosamax may be associated with certain atypical femoral fractures, and proposed a label change to warn about that risk. The FDA said no. It formally denied the proposal without suggesting (much less mandating) any alternative. Respondents then sued under state law, alleging that Merck failed to warn about this risk.

Two district judges correctly found that the FDA's order denying Merck's request preempted the claims. After all, a company cannot be held liable if federal law made it impossible to comply with state law—which the FDA itself agreed was true here. But the Third Circuit twice reversed. This Court granted certiorari last time to reject the Third Circuit's analysis. It should do so again, because the panel defied this Court's ruling—gutting drug preemption and rendering itself an outlier among the Circuits.

Last time, the Third Circuit thought Merck needed a "smoking gun" sufficient to convince a jury, by "clear and convincing evidence," it could not have obtained FDA approval. *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 286, 294 (3d Cir. 2017) (*Fosamax I*). Every Member of this Court rejected that approach. *Merck Sharp & Dohme Corp. v. Albrecht*, 587 U.S. 299, 315-18 (2019). The Court clarified that preemption is a question for judges, who must assess the meaning of agency action (including by resolving any subsidiary factual disputes) with no thumb on the scale. It set forth a clear, two-part test for preemption in a case like this one: The manufacturer must prove (1) "that it fully informed the FDA of the justifications for the warning required

by state law"; and (2) "that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning." *Id.* at 314. Making that showing establishes impossibility. *See id.*

On remand, the district court applied that two-part test. Based on both a thorough record review and the statutory and regulatory context, the judge found that Merck fully informed the FDA about the risk, and that the agency's "no" to the proposed warning really meant "no." So it would have been impossible for Merck to abide by the alleged state-law duty without running afoul of federal law. The claims were thus preempted under this Court's test.

After *Albrecht*, the Third Circuit could no longer punt to a jury. Nor did the panel identify any error in the district court's factual findings, or reject its construction of the FDA's order as a matter of law. Instead, the panel discerned what it dubbed a "heavy *Albrecht* presumption"—a new rule under which any "ambiguity" in the record itself defeats preemption. Pet.App.66a. Thus, a manufacturer cannot prevail merely by offering the *best* interpretation of the FDA's action—it must offer the *only possible* interpretation, without considering extrinsic evidence. Put another way, the court must defer to the plaintiffs' bar about what the FDA did, even where (as here) the FDA itself disagrees. That is baseless. *Albrecht* imposes no such "presumption." No other Circuit has construed it this way. Instead of *applying* this Court's test, the Third Circuit made up a way to *bypass* it. In doing so, it repackaged the same "smoking gun" rule this Court rejected last time—demanding "abundantly clear" evidence on the face of the FDA's denial order.

Making matters worse, the court below also flouted Justice Alito's *Albrecht* concurrence, which the Chief Justice and Justice Kavanaugh joined, that explained the "highly relevant" statutory context for FDA actions that must be "considered" in the preemption inquiry. 587 U.S. at 325 (Alito, J., concurring in judgment). In particular, the agency now has a statutory obligation to mandate label revisions when it believes they are scientifically warranted. If an informed FDA rejects a proposed warning about a risk without directing an alternative, the only possible inference is thus that it did not think one was needed. Yet the Third Circuit indulged the theory that the FDA had rejected Merck's proposal on *semantic* grounds. While the Third Circuit purported to "consider" the legal context that Justice Alito's concurrence had flagged, it did so only to deem it *irrelevant*. Pet.App.70a-75a. In this respect too, the Third Circuit departed from how all other courts have analyzed preemption after *Albrecht*.

In short, the decision below precludes using *factual* or *legal* context to construe FDA labeling decisions. That strips courts of the ability to perform the task this Court assigned them. And it puts manufacturers in an impossible position. Even if one tries to warn and is thwarted by the FDA, plaintiffs' lawyers will always be able to offer some argument that the denial *might* not have reflected a conclusive rejection—that the FDA *might* have approved a different warning that *might* have satisfied state law. Manufacturers will have no choice but to pester the FDA, add unnecessary warnings at the risk of federal sanctions, or submit to state-law liability. That is not fair to manufacturers. It is not good for patients. And it is not consistent with the Supremacy Clause.

This Court reviewed the Third Circuit's last decision due to "[t]he importance of the pre-emption issue" to the pharmaceutical industry and all who rely on it. *Wyeth v. Levine*, 555 U.S. 555, 563 (2009); *see also Albrecht*, 587 U.S. at 310. The Circuit's equally flawed redo warrants review for the same reason.

OPINIONS BELOW

The district court opinion granting Merck summary judgment (Pet.App.77a) is reported at 593 F. Supp. 3d 96. The Third Circuit's opinion vacating that order (Pet.App.1a) is reported at 118 F.4th 322.

JURISDICTION

The Third Circuit entered judgment on September 20, 2024, and denied Merck's timely rehearing petition on November 19, 2024. Pet.App.1a, Pet.App.169a. Justice Alito extended the time to file this petition. 24A720. 28 U.S.C. § 1254(1) confers jurisdiction.

PROVISIONS INVOLVED

Relevant statutory and regulatory provisions are reproduced at Pet.App.171a-212a.

STATEMENT

A. Statutory and Regulatory Background

Congress and the FDA have crafted a regulatory regime in which drug manufacturers and the agency work hand-in-hand to warn patients of the risks inherent in taking beneficial medicines. Although "the manufacturer bears responsibility for the content of its label at all times," *Wyeth*, 555 U.S. at 570-71, the FDA plays a central role in label approvals and revisions. "FDA regulations set out requirements for the content, the format, and the order of the safety information on the drug label." *Albrecht*, 587 U.S. at 304.

Those regulations appreciate that warnings are not an unalloyed good. Rather, excessive label warnings could "discourage appropriate use of a beneficial drug" and "decrease the usefulness and accessibility of important information by diluting or obscuring it." 73 Fed. Reg. 2848, 2851 (Jan. 16, 2008). Accordingly, any label warning must meet specific scientific criteria. FDA regulations set a "hierarchy of label information," from "prominent 'boxed' warnings about risks that may lead to death or serious injury"; to "warnings and precautions about other potential safety hazards"; to mere "adverse reactions." *Albrecht*, 587 U.S. at 304. To revise the Warnings & Precautions portion, there must be "reasonable evidence of a causal association" between the drug and the health risk. 21 C.F.R. § 201.57(c)(6)(i). To add to the Adverse Reactions list, there need only be "some basis to believe there is a causal relationship." *Id.* § 201.57(c)(7).

"Prospective drug manufacturers work with the FDA to develop an appropriate label when they apply for FDA approval of a new drug." *Albrecht*, 587 U.S. at 304. The FDA may grant such approval "only if it determines that the drug … is safe for use under the conditions of use prescribed, recommended, or suggested in [its] proposed labeling." *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 476 (2013). After approval, the FDA monitors the drug and its label in concert with the manufacturer, who must investigate and report any serious, unexpected adverse events, *see* 21 C.F.R. § 314.80(c)(1)(i), and also must annually report "significant new information … that might affect the safety, effectiveness, or labeling of the drug," *id.* § 314.81(b)(2)(i).

Once a drug hits the market, there are only two ways in which the manufacturer may revise its label. *First*, the manufacturer may submit a Prior Approval Supplement (PAS) seeking advance permission for the change from the FDA. *See id.* § 314.70(b). *Second*, the Changes Being Effected (CBE) regulations "permit[] drug manufacturers to change a label without prior FDA approval if the change is designed to 'add or strengthen a ... warning' where there is 'newly acquired information' about the 'evidence of a causal association' between the drug and a risk of harm." *Albrecht*, 587 U.S. at 305 (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A)). The required level of scientific evidence of causation is the same as set forth above—"reasonable evidence" for the Warnings & Precautions section, and "some basis to believe" for the Adverse Reactions—regardless of which regulatory mechanism is used for the revisions. *See* 73 Fed. Reg. 49603, 49604-05 (Aug. 22, 2008).

Since 2007, Congress has also obligated the FDA to independently ensure that drug labels reflect current science. If the agency learns of "new information" that "should be included in the labeling," it "shall promptly notify" the manufacturer. 21 U.S.C. § 355(*o*)(4)(A). And if the FDA "disagrees with the [manufacturer's] proposed changes … or with the statement setting forth the reasons why no labeling change is necessary," it "shall initiate discussions to reach agreement on whether the labeling … should be modified to reflect the new safety information, and if so, the contents of such labeling changes." *Id.* § 355(*o*)(4)(C). Ultimately, the FDA "may issue an order directing … a labeling change as [it] deems appropriate." *Id.* § 355(*o*)(4)(E).

Consistent with this obligation, the FDA works with manufacturers to approve and revise labels. If the FDA identifies "easily correctable deficiencies," then it "make[s] every reasonable effort to communicate" them "promptly" so the applicant can "correct" them. 21 C.F.R. § 314.102(b). And "if the only deficiencies" concern "editorial or similar minor deficiencies in the draft labeling," the FDA "will approve" the application "conditioned upon the applicant incorporating the … changes." *Id.* § 314.105(b). These principles guide the FDA's review of label changes through the CBE and PAS processes alike. *See id.* § 314.71(b)-(c)

If the FDA determines to *deny* a label proposal, it will issue a Complete Response Letter (CRL), which "describe[s] all of the specific deficiencies that the agency has identified" and, "[w]hen possible," "recommend[s] actions that the applicant might take to" secure approval. *Id.* § 314.110(a)(1), (a)(4). A CRL "reflects [the] FDA's complete review of the data submitted." *Id.* § 314.110(a)(2). While the FDA may bypass an evaluation of "proposed product labeling" if it has already determined "that the data submitted are inadequate to support approval," *id.* § 314.110(a)(3), the reverse is not true: The FDA cannot reject a label revision based solely on its *wording* without considering whether a warning is warranted based on the new scientific data. *See* 73 Fed. Reg. 39588, 39592 (July 10, 2008).

B. Factual Background

1. Merck's drug Fosamax "treats and prevents osteoporosis in postmenopausal women." *Albrecht*, 587 U.S. at 305. Like other bisphosphonates, Fosamax works by slowing the deleterious process that occurs

in bones of post-menopausal women, helping patients retain bone mass, maintain bone strength, and avoid fractures. *See id.* But, by hypothesis, the "mechanism through which Fosamax decreases the risk of osteoporotic fractures may increase the risk of a different type of fracture." *Id.* "[A]ll bones—healthy and osteoporotic alike—sometimes develop microscopic cracks that are not due to any trauma, but are instead caused by the mechanical stress of everyday activity." *Id.* "Those so-called 'stress fractures' ordinarily heal on their own through the bone remodeling process. But, by slowing the breakdown of old bone cells, Fosamax and other bisphosphonates may cause stress fractures to progress to complete breaks." *Id.* Of particular concern are "atypical femoral fracture[s]"—rare fractures that occur in a specific part of the femur, with only minimal trauma. *Id.*; C.A.App.1118.

2. Merck "brought those theoretical considerations to the FDA's attention" during the approval process, but the agency approved Fosamax in 1995 without any warning of the risk. *Albrecht*, 587 U.S. at 306.

In March 2008, Merck submitted a safety update with "over 30 pages of information regarding atypical femur fractures and suppression of bone turnover," noting that "recent publications" "implicated a link between prolonged bisphosphonate therapy and atypical low-energy non-vertebral fractures." *Fosamax I*, 852 F.3d at 275. By June 2008, the FDA told manufacturers it was "aware of reports regarding the occurrence of … hip fractures in patients using bisphosphonates" and was "concerned about this developing safety signal." *Id.* It asked for additional materials by July; "Merck promptly complied." *Id.*

In September 2008, Merck submitted a PAS seeking approval to revise Fosamax's label to account for the risk that the FDA had inquired about. *See id.* at 276; Pet.App.87a. While existing data did not "establish whether treatment with" Fosamax actually "increases the risk of [these] ... low-energy subtrochanteric and/or proximal shaft fractures," Merck explained that it was "important to include an appropriate statement about them in the product label" to "increase physicians' awareness of possible fractures" and encourage "early intervention" to "possibly prevent[] the progression to complete fracture and/or other complications." C.A.App.1349; *Fosamax I*, 852 F.3d at 276.

Merck sought to revise the label in two ways. *First*, it sought to add "low-energy femoral shaft fracture" to the list of Adverse Reactions. C.A.App.1292. *Second*, it sought to add the following supplement to the Warnings & Precautions section:

> **Low-Energy Femoral Shaft Fracture**
>
> Low-energy fractures of the subtrochanteric and proximal femoral shaft have been reported in a small number of bisphosphonate-treated patients. Some were stress fractures (also known as insufficiency fractures) occurring in the absence of trauma. Some patients experienced prodromal pain in the affected area, often associated with imaging features of stress fracture, weeks to months before a complete fracture occurred. The number of reports of this condition is very low, and stress fractures with similar clinical features also have occurred in patients not treated with bisphosphonates. Patients with suspected

> stress fractures should be evaluated, including evaluation for known causes and risk factors (e.g., vitamin D deficiency, malabsorption, glucocorticoid use, previous stress fracture, lower extremity arthritis or fracture, extreme or increased exercise, diabetes mellitus, chronic alcohol abuse), and receive appropriate orthopedic care. Interruption of bisphosphonate therapy in patients with stress fractures should be considered, pending evaluation of the patient, based on individual benefit/risk assessment.

Pet.App.19a-20a.

In support, "Merck submitted a lengthy analysis of femoral fractures in Fosamax users, cited to nine articles on such cases, and summarized the findings in a clinical overview." Pet.App.88a. Merck explained that it used the term "stress fracture" to refer to "low-energy subtrochanteric/mid femoral shaft fractures" that occurred with no "identifiable external trauma." C.A.App.1311-12.

3. On May 22, 2009, the FDA denied the proposed warning in a CRL signed by Dr. Scott Monroe. It "agree[d] that atypical and subtrochanteric fractures should be added" to the Adverse Reactions section (which requires only "some basis to believe" in a causal link), though it revised the phrasing. C.A.App.1152-53. But it rejected Merck's Warnings & Precautions proposal (with its higher "reasonable evidence of a causal association" standard). In the CRL—which must identify every deficiency in the application—the FDA explained that it rejected the Warnings proposal for three "reasons" (in the plural):

> [1] [Y]our justification for the proposed PRECAUTIONS section language is inadequate. [2] Identification of "stress fractures" may not be clearly related to the atypical subtrochanteric fractures that have been reported in the literature. [3] Discussion of the risk factors for stress fractures is not warranted and is not adequately supported by the available literature and post-marketing adverse event reporting.

Pet.App.22a (brackets added).

That split decision—rejecting a Warnings revision about atypical fractures, but agreeing to list them as an Adverse Reaction—tracked Merck's back-and-forth with FDA officials. In April 2009, an official informed Merck by email that the FDA "would only approve a reference to atypical fractures in the 'Adverse Reaction' section." *Fosamax I*, 852 F.3d at 277. "If Merck agree[d] to hold off on the W[arnings] & P[recautions] language at this time, then [the FDA] c[ould] go ahead and close out these supplements," and could later work out "language for a W[arnings] & P[recautions] atypical fracture language, if it is warranted." C.A.App.1150. Merck's contemporaneous notes from an April 2009 call also reflect Dr. Monroe's preview that "the FDA could agree to additional language in the Adverse Reactions section" but "likely would not approve similar language in the Precautions section." Pet.App.88a; C.A.App.1250-51. "In [Dr. Monroe's] view, Merck's 'elevation' of the warning to a Precaution was 'prolonging' approval" because "the conflicting nature of the literature d[id] not provide a clear path forward." Pet.App.89a.

Merck eventually acquiesced, followed the FDA's instruction to "withdraw" the PAS, and submitted a CBE that (over noted objection) revised only the list of Adverse Reactions, as directed. Pet.App.91a.

4. Thereafter, the FDA continued to publicly state (including in an official Drug Safety Communication in March 2010) that "the data" showed no "clear connection" between atypical femur fractures and bisphosphonate use; indeed, its review "did not show an increase in this risk in women using these medications." C.A.App.1160. But the FDA also noted that it was "working closely with outside experts," including members of a "recently convened" expert Task Force, "to gather additional information that may provide more insight into this issue." *Id.*

That Task Force published a report in September 2010, finding "evidence of a relationship between long-term [bisphosphonate] use and a specific type of subtrochanteric and femoral shaft fracture." *Fosamax I*, 852 F.3d at 278. While the data did not "establish" "a causal association," the Task Force recommended (just as Merck had) that "[p]hysicians and patients … be made aware" of the risk. C.A.App.1058. An FDA official told the press that the Task Force report had made the agency more "'confident' that atypical femur fractures are 'potentially more closely related to' long-term use of bisphosphonates" than it "'previously had evidence for.'" *Id.* As a result, the FDA declared it would *now* be "considering label revisions." *Id.* And it promptly proposed a new warning that "[a]typical, low-energy, or low trauma fractures of the femoral shaft have been reported in bisphosphonate-treated patients," while cautioning that "[c]ausality has not been established." Pet.App.24a.

To help doctors spot the issue early, Merck proposed edits that "referred to the risk of 'stress fractures.'" Pet.App.93a. But the FDA was concerned that "'for most practitioners, the term "stress fracture" represents a minor fracture and this would contradict the seriousness of the atypical femoral fractures associated with bisphosphonate use.'" *Id.* So the agency rejected Merck's redline, and Merck added the FDA's original language to Fosamax's label, where it remains to this day. Pet.App.25a.

C. Procedural Background

1. Hundreds of Fosamax users who had allegedly suffered atypical fractures sued Merck. Each plaintiff alleged that Merck had failed to warn about this risk, including by omitting it from the Warnings & Precautions section of the label before late 2010. Some 1,200 cases were sent to an MDL in the District of New Jersey. *See Fosamax I*, 852 F.3d at 279.

After a bellwether trial, the district court (Pisano, J.) entered summary judgment for Merck based on impossibility preemption. *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 951 F. Supp. 2d 695, 700 (D.N.J. 2013). The court found that "the evidence … establishe[d] that the FDA would not have approved a label change to the Precautions section of the Fosamax label" before September 2010 (when the Task Force report turned the tide). *Id.* at 703. Judge Pisano later extended that ruling across the MDL. As he put it: There was "clear evidence that the FDA *would have* rejected a stronger Precautions warning because the FDA *did* reject a stronger Precautions warning." *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 2014 WL 1266994, at *16 (D.N.J. Mar. 26, 2014).

2. The Third Circuit vacated and remanded. To satisfy *Wyeth*, it held, a "manufacturer must prove that the FDA would have rejected a warning not simply by a preponderance of the evidence, … but by 'clear evidence,'" which it equated with "clear and convincing evidence." *Fosamax I*, 852 F.3d at 285-86. The court also held that a *jury* must act as factfinder for this inquiry. *Id.* at 293. So a manufacturer could not prevail absent a "'smoking gun' rejection letter from the FDA" that would leave a jury no choice but to find that the manufacturer could not have secured FDA approval for a label change. *Id.* at 294.

Despite acknowledging the robust evidence of just that, the Third Circuit ultimately held that a "jury could find it less than highly probable that the FDA would have rejected" a warning, had Merck proposed different language. *Id.* at 294, 297. The court said that a jury could indulge the notion that perhaps the FDA had rejected Merck's proposal solely because it referred to "stress fractures," a phrase the FDA later explained might confuse doctors. *See id.* Given that possibility, and the "heightened standard of proof," Merck could not establish preemption. *Id.* at 299.

3. This Court vacated and remanded. It held that preemption is a legal issue that must be decided by "a judge, not the jury"—even when it requires answering "factual questions" about "the meaning and scope" of FDA action or "what information the FDA had before it." *Albrecht*, 587 U.S. at 310, 317. The Court also held that no heightened standard applies to this analysis: Contrary to the Third Circuit's misunderstanding, *Wyeth*'s reference to "clear evidence" did not impose an "evidentiary standard[]," *id.* at 315, but was simply a description of the applicable test.

The Court took the opportunity to clarify that test. In a case like this, the manufacturer must show that it "fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Id.* at 303. Those showings establish "that federal law prohibited [it] from adding a warning that would satisfy state law." *Id.* at 314.

The FDA participated at both the certiorari stage (at this Court's invitation) and the merits stage. It agreed that Respondents' claims were preempted, because Merck "provided FDA with the relevant scientific data about Fosamax's risks," C.A.App.1517, and the FDA "rejected" Merck's proposed revisions "because the data at that time was insufficient to justify a change," C.A.App.1523-24—*not* because of semantic issues with the "proposed text," C.A.App.1504-05. Thus, the FDA agreed that federal law forbade Merck from revising its label before September 2010. C.A.App.1505.

Writing for three Justices, Justice Alito concurred in the judgment. He emphasized the importance of 21 U.S.C. § 355(*o*)(4)(A), which "imposed on the FDA a duty to initiate a label change" when it learns of "'new information, including any new safety information,'" that requires warnings. 587 U.S. at 324. That duty is "highly relevant": Given the presumption of regularity, "if the FDA declines to require a label change despite having received and considered information regarding a new risk, the logical conclusion is that the FDA determined that a label change was unjustified." *Id.* at 324-25. Justice Alito "assume[d] that the Court of Appeals [would] consider the effect of § 355(*o*)(4)(A)" on remand. *Id.* at 325.

4. The Third Circuit remanded for the district court "to determine … whether the plaintiffs' state law claims are preempted." Pet.App.97a. The district court (Wolfson, C.J.), then issued an 87-page opinion finding this Court's two-part preemption test satisfied.

On the first prong, Judge Wolfson found that Merck had "fully informed the FDA of the justifications for the warning required by state law." Pet.App.110a. "Between its formal safety updates, periodic emails, and PAS," Merck "clearly and fully informed the FDA of the panoply of risks associated with long-term Fosamax use and the justifications for its proposed label change." Pet.App.113a.

On the second prong, the court observed that the CRL's text "g[ave] rise to competing inferences with respect to why the FDA rejected [Merck's] warning," and thus sought "to ascertain its meaning and scope." Pet.App.141a. Contextual evidence confirmed that the FDA rejected Merck's warning because it "doubted the evidence linking bisphosphonate use to atypical femoral fractures in a causal sense." Pet.App.148a. "FDA's communications" (*id.*) around the time of the CRL supported that reading (Pet.App.141a-145a), as did its subsequent actions (Pet.App.145a-146a, 152a), the statutory and regulatory structure (Pet.App.148a-153a), and the FDA's representations in this Court (Pet.App.146a-148a). The court rejected Respondents' theory that the FDA "expos[ed] patients to the risk of severe injury" just because it "perceived" (but declined to correct) an easily fixable "problem" with Merck's "language, *i.e.*, stress fracture." Pet.App.150a. Rather, the FDA "informed [Merck] that it would not approve changing the Fosamax label to include" Respondents' desired warning. Pet.App.79a.

5. The Third Circuit *again* vacated and remanded.

The court agreed that the first *Albrecht* prong was satisfied: Judge Wolfson "did not err in finding that Merck fully informed the FDA of the justifications for adding to the Fosamax label a warning about atypical femoral fractures," and Respondents' claim that Merck "provided misleading information" "stretche[d] credulity." Pet.App.44a-45a, 52a-53a.

On the second *Albrecht* prong, the panel dismissed Respondents' suggestion that the CRL had rejected a warning about a *different risk*—of "'garden-variety' stress fractures." Pet.App.54a. There was no "basis to believe that the FDA did not understand that Merck was proposing a warning about atypical femoral fractures." Pet.App.55a. Nonetheless, the panel held that the FDA's rejection of that proposal did not do the trick. Like the district court, the Third Circuit viewed the CRL as facially "ambiguous": It could certainly be read as rejecting Merck's proposed warning based on "a lack of scientific support," but it could alternatively be construed as a rejection of Merck's use of "the term 'stress fractures.'" Pet.App.61a-62a. Unlike the district court, however, the Third Circuit refused to try to *resolve* that ambiguity and thus identify the *correct* interpretation of what federal law required.

Rather, the panel held, "the strong presumption [against preemption] that the Supreme Court has established will likely be determinative" in any "close case." Pet.App.62a. While "not unsympathetic to the pressures Merck faced from the competing demands" of federal and state law, the court thought its hands were tied: Because of "the 'presumption against pre-emption,'" it "'ha[d] a duty to accept the reading [of the

CRL] that disfavors pre-emption.'" Pet.App.64a-65a. With "the ambiguities" thus "swept away by the heavy *Albrecht* presumption," the Third Circuit cast aside the district court's review of the "extrinsic evidence" as "[un]necessary." Pet.App.66a.

Only *after* concluding that the CRL's ambiguity defeated preemption did the Third Circuit consult the statutory context. It found that the FDA's failure to propose an alternative warning was irrelevant. The FDA was still "deciding whether a change … was needed," the court concluded, so its rejection of Merck's proposal did not mean the agency had conclusively determined that such a warning did *not* meet scientific standards for inclusion (thus triggering preemption)—or, that it *did* meet those standards (thus triggering the FDA's duty to act). Pet.App.72a-73a.

Merck's petition for panel rehearing explained why the panel's discussion of § 355(*o*)(4) made no sense: If the FDA was "not fully convinced of the link" between Fosamax and atypical fractures when it rejected Merck's proposal, Pet.App.71a, then Merck was barred from adding a warning until new evidence emerged. The panel denied rehearing without comment.

REASONS FOR GRANTING THE PETITION

For the second time in this long-running litigation, the Third Circuit issued a flawed decision that guts preemption. Indeed, that court effectively revived the troubling ruling that this Court vacated just six years ago—replacing its old "clear and convincing" test with a new "heavy presumption." Given the "importance of the pre-emption issue" to the pharmaceutical industry and all who rely on it, *Wyeth*, 555 U.S. at 563, this Court should again intervene.

The Third Circuit defied *Albrecht*, making itself an outlier among the Courts of Appeals yet again. In *Albrecht*, this Court articulated a two-step preemption test and assigned its application to judges. It did not layer on an extra "presumption" or call for any thumb on the scale. To the contrary, *Albrecht* clarified that impossibility preemption—while "demanding" in substance—is *not* governed by any special heightened procedures. No other Circuit has even mentioned an evidentiary "presumption" that the FDA denies label revisions for *non*-preemptive reasons. Nor has any other Circuit refused to consider extrinsic evidence.

The court also thumbed its nose at Justice Alito's *Albrecht* concurrence. As he explained, manufacturers and courts are entitled to presume that the FDA does not flout its statutory duty to protect public health. So if, as here, the FDA denies a warning proposal without directing an alternative, that means the agency does not believe a warning is justified. That makes adding a warning impossible. Yet the panel refused to follow this simple logic. Here too, the Third Circuit stands alone: No other court has so casually sidelined legal context.

In the end, the Third Circuit's approach makes it impossible to comply with both federal and state law. If courts cannot consult the facts (extrinsic evidence) or the law (statutory and regulatory context) to resolve ambiguity in FDA actions, that puts manufacturers in a pickle. After all, creative plaintiffs can always devise ambiguity and speculate about counterfactuals. That leaves manufacturers to hope they are not sued or to pester their regulator with requests to overwarn. This regime is untenable for manufacturers, patients, and the FDA alike. This Court's review is needed.

I. THE THIRD CIRCUIT DEFIED *ALBRECHT* AND MADE ITSELF A PREEMPTION PARIAH ONCE AGAIN.

The Court should grant certiorari because the Third Circuit defied this Court's prior decision *in this very case*—and, in doing so, made itself a pariah.

First, the Third Circuit clung stubbornly to the notion that a manufacturer asserting impossibility preemption faces unusually high evidentiary hurdles. Last time, it imposed a clear-and-convincing-evidence standard. This time, it devised a novel rule that the evidence must be "abundantly clear," because any "ambiguity" defeats preemption at the outset, even if context would resolve it. Nothing in *Albrecht* permits putting that thumb back on the scale. Nor has any other Circuit done anything like this; they all do what courts always do—review the full record to evaluate whether the applicable test has been met.

Second, the Third Circuit missed the point of Justice Alito's concurrence. Statutory and regulatory context are vital tools for interpreting FDA actions, and they foreclose assuming that the agency flouted its duty to warn patients of substantiated risks. Other courts have recognized this. But the court below held that Merck could be liable even as the FDA flatly denied its proposal without directing any alternative warning.

A. Instead of Applying This Court's Test, the Panel Adopted a Baseless Presumption.

Last time, this Court granted review to clarify the contours of *Wyeth*'s preemption test "[i]n light of … uncertainties" concerning its application. *Albrecht*, 587 U.S. at 310. The Court did so chiefly by correcting the Third Circuit's errors. But on remand, that court repeated virtually identical mistakes.

1. In *Wyeth*, this Court considered the preemptive effect of federal drug labeling law on state-law failure-to-warn liability. On the one hand, the Court rejected the claim that state law is preempted "[o]nce the FDA has approved a drug's label, … regardless of whether there is any evidence that the FDA has considered the stronger warning at issue." 555 U.S. at 573-74. If new scientific evidence emerges, the CBE regulations allow a manufacturer to strengthen a warning without prior approval. *See id.* at 569-71. Thus, the "mere fact that the FDA approved [a defendant's] label" is not enough to create impossibility. *Id.* at 573. On the other hand, the Court agreed that if the FDA would *not* approve a label revision, that would preempt claims premised on the same risk. So, the Court held, preemption applies only if there is "clear evidence that the FDA would not have approved a change." *Id.* at 571.

Albrecht clarified the *Wyeth* test in three ways. *First*, it articulated a two-pronged showing sufficient to satisfy the test: *Wyeth*'s "'clear evidence' is evidence that" (1) the "manufacturer fully informed the FDA of the justifications for the warning" and (2) the FDA "informed the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning." *Albrecht*, 587 U.S. at 303. A manufacturer that makes those showings establishes that federal law made it impossible to comply with state law.

Second, *Wyeth*'s reference to "clear evidence" did *not* impose a heightened "evidentiary standard[]," such as "clear and convincing evidence." *Id.* at 315. Instead, the phrase is shorthand for the conceptually narrow circumstance in which the federal labeling regime and state tort law "irreconcilably conflict"—*i.e.*, where the two elements above are satisfied. *Id.*

Finally, the task of determining whether a conflict exists belongs to judges, not juries. *Id.* And a judge makes that determination by "evaluat[ing] the nature and scope of [the] agency's determination"—just as courts often "interpret agency decisions in light of the governing statutory and regulatory context." *Id.* at 316. While this inquiry is fundamentally legal, some "subsidiary factual disputes" may arise, and the court is tasked with resolving those too. *Id.* at 317 (drawing analogy to "construction of patent claims").

2. On remand, the district court carried out the task *Albrecht* assigned to it. The court reviewed the record, resolved subsidiary factual disputes, and issued an 87-page analysis concluding that both *Albrecht* prongs were met. As relevant here, the court construed the CRL as a rejection of *any* atypical fracture warning, based on the FDA's determination that the scientific data did not yet show enough evidence of causation. The court drew that inference from the FDA's actions and statements at the time, as well as from its express representations in its *Albrecht* amicus briefs.

On appeal, the Third Circuit identified no reversible error in Judge Wolfson's factual findings. Nor did it determine as a matter of law that her interpretation of the CRL was inferior to Respondents' alternative reading (under which the FDA merely objected to Merck's use of the term "stress fracture"). Instead, the Third Circuit invented this novel legal rule: The preemption test must be applied with a thumb on the scale against defendants, because "the 'presumption against pre-emption'" assigns courts "'a duty to accept the reading'" of the FDA's actions "'that disfavors pre-emption.'" Pet.App.65a. So the preemptive effect of an FDA action must be "abundantly clear" before a

manufacturer can prevail—or, in other words, an ambiguous record "will seldom, if ever, be enough to overcome the presumption." Pet.App.66a. That "heavy *Albrecht* presumption" meant the district court had erred just by *trying* to interpret the CRL using "extrinsic evidence." *Id.* Apparently, the court's new presumption is unrebuttable to boot.

In sum, the Third Circuit saw no need to identify the *best* interpretation of the CRL. Merck's reading was not the *only* reading consistent with the face of the FDA's order, so preemption was off the table; indeed, it was reversible error to inquire further. Courts must now defer to *plaintiffs'* interpretations of FDA action—even when, as here, all extrinsic evidence *plus the FDA itself* say the opposite.

3. That approach cannot be squared with *Albrecht*, or with this Court's other precedents.

Tellingly, while the opinion below called its novel rule the "heavy *Albrecht* presumption," this Court in *Albrecht* never even used the term "presumption." It instead clarified that impossibility preemption—while "demanding" in *substance*—is in *process* a run-of-the-mill exercise in interpreting federal agency action. Nothing in *Albrecht* permits, much less directs, courts conducting the inquiry to pull the plug once a plaintiff identifies an ambiguity. To the contrary, *Albrecht* expressly *rejected* the idea that courts applying its test must do so with a thumb on the scale against preemption. *See* 587 U.S. at 314-15. Indeed, that is why the Court rejected the Third Circuit's clear-and-convincing-evidence test. But it is hard to see any difference between that and this new "presumption" requiring "abundantly clear" evidence.

Quite remarkably, the Third Circuit based its new "presumption" on the same wisp of precedent as its clear-and-convincing-evidence test—*Wyeth*'s reference to "clear evidence"—even after this Court disabused it of this misunderstanding. *Albrecht* explained that "clear evidence" simply "*is*" evidence that satisfies the test's demanding substantive elements. 587 U.S. at 303 (emphasis added); *see also id.* at 325 (Alito, J., concurring in judgment) (calling that *Wyeth* language "merely a rhetorical flourish"). Yet the court below confessed that it had a hard time "get[ting] away from *Wyeth*'s statement … that 'clear evidence' is required" when determining "just how much proof … is enough" to "persuade." Pet.App.68a.

Stepping back, the Third Circuit committed a basic category error by invoking the "presumption against preemption" here at all. In impossibility cases, federal law either permits compliance with state law or does not; there is no reason to presume one way or the other. Indeed, as a *non obstante* provision, the Supremacy Clause does not allow courts to "distort federal law"—in *either* direction—"to accommodate conflicting state law." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 623 (2011) (plurality op.). That is why this Court's impossibility-preemption cases have typically *not* relied on presumptions. *Compare id.* at 624 n.8 (rejecting appeal to presumption by explaining that "possibility of *possibility*" does not "defeat[] pre-emption"), *with id.* at 638 (Sotomayor, J., dissenting) (emphasizing role of presumption); *compare Bartlett*, 570 U.S. at 479-80 (outlining doctrine without mentioning presumption), *with id.* at 498 n.1 (Sotomayor, J., dissenting) (criticizing "majority's failure to adhere to the presumption").

To be sure, *Wyeth* did mention the presumption in a footnote, to ground its assumption that Congress does not disturb "the historic police powers of the States." 555 U.S. at 565 & n.3. That interpretive principle helps explain *Wyeth*'s holding that the "FDA's power to approve or to disapprove labeling changes" does not, "*by itself*, pre-empt[] state law." *Albrecht*, 587 U.S. at 311. But this Court *never* treated that "presumption" as a procedural rule that governs *how* a court must apply a given preemption test to the record before it.

The decision below thus rests on a fundamental misunderstanding of the role of the "presumption against preemption" in cases like this one. The assumption that Congress does not ordinarily intend to displace state law gave rise to the demanding *Wyeth-Albrecht* test in the first place. To *also* wield the presumption as an evidentiary cudgel against defendants when *applying* that test double-counts it. In short, a defendant like Merck who makes *Albrecht*'s twin showings *overcomes* the presumption—its efforts to do so are not subject to special judicial skepticism.

4. No other Circuit has adopted or even suggested the evidentiary "presumption" that the Third Circuit created below. Instead, other courts do the *Albrecht* analysis the same way they apply other legal tests—straight, and based on the record as a whole.

To illustrate: In a pre-*Albrecht* decision, the Seventh Circuit relied on evidence of "discussions between the FDA" and the manufacturer to reject an argument that the agency had turned down a warning based on a disagreement about *where* it should appear on the drug's label. *Dolin v. GlaxoSmithKline LLC*, 901 F.3d 803, 814 (7th Cir. 2018). After *Albrecht*, the plaintiff

moved to set aside the judgment under Rule 60(b)(6), but the Seventh Circuit held that its decision was fully consistent with *Albrecht*'s understanding of the "clear evidence" test. *See Dolin v. GlaxoSmithKline LLC*, 951 F.3d 882, 889-91 (7th Cir. 2020). Neither decision applied anything akin to the Third Circuit's "heavy *Albrecht* presumption." Pet.App.66a.

The First Circuit likewise did not discuss any "presumption" or heightened standard when it applied *Albrecht*—instead, it recognized that "clear evidence" simply "entail[s]" the two substantive showings that a manufacturer must make to prove preemption. *In re Zofran (Ondansetron) Prods. Liab. Litig.*, 57 F.4th 327, 341 (1st Cir. 2023). And to assess (and reject) an argument that the manufacturer had enough "newly acquired information" to invoke the CBE process, the court carefully evaluated scientific studies, without any thumb on the scale. *See id.* at 337-39.

In post-*Albrecht* decisions on that newly acquired evidence issue—to which the "presumption" adopted below would logically apply—the Second, Fourth, and Fifth Circuits did the same. Each court scrutinized the record to assess whether the proffered information was "newly acquired," without suggesting that it must construe the record against preemption or blind itself to context. *See Hickey v. Hospira, Inc.*, 102 F.4th 748, 757-59 (5th Cir. 2024) (per curiam); *Knight v. Boehringer Ingelheim Pharms., Inc.*, 984 F.3d 329, 338-41 (4th Cir. 2021); *Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 708-09 (2d Cir. 2019). To the contrary, the Fourth Circuit "caution[ed] against a quick trigger," calling instead for "[a] careful review of the record" before deciding preemption. *Knight*, 984 F.3d at 340-41.

In all of these cases, the plaintiffs offered plausible interpretations of the record that raised the *possibility* of consistency between federal and state law. But until the decision below, courts perceived no "duty" to blindly *accept* those interpretations. Pet.App.65a. Instead, they conducted *Albrecht*'s preemption test with the same rigor and care applicable to other cases. *See, e.g.*, *In re Incretin-Based Therapies Prods. Liab. Litig.*, 524 F. Supp. 3d 1007, 1029-33 (S.D. Cal. 2021), *aff'd on other grounds*, No. 21-55342, 2022 WL 898595 (9th Cir. Mar. 28, 2022) (holding that manufacturer satisfied *Albrecht* after exhaustive review of record, including extrinsic evidence); *Ridings v. Maurice*, 444 F. Supp. 3d 973, 998 (W.D. Mo. 2020) (finding preemption "in light of the known issues [with the science] and the ongoing give-and-take" between manufacturer and FDA). *Albrecht* demands nothing less—as everyone but the Third Circuit seems to recognize.

B. The Third Circuit Also Ignored Statutory and Regulatory Context.

The panel appears to have felt squeamish about using extrinsic evidence to construe agency action. It should not have. Evaluating "the nature and scope of an agency's determination" may require looking to the full record, beyond the four corners of the order itself. *Albrecht*, 587 U.S. at 316. But, at minimum, there can be no objection to using the "governing statutory and regulatory context" as an interpretive tool. *Id.* Justice Alito highlighted its power in his concurrence. Indeed, it slices through the Gordian knot in cases like this. Yet the Third Circuit—again departing from all other courts—failed to heed Justice Alito's instruction. This error underscores the need for renewed review.

1. In a provision that took effect after the injury at issue in *Wyeth*, Congress required the FDA to initiate discussions and mandate label changes if it "becomes aware of new information" that "should be included in the labeling." 21 U.S.C. § 355(*o*)(4)(A). As Justice Alito explained in *Albrecht*, that duty, coupled with the presumption of regularity, means that when "the FDA declines to require a label change," the "logical conclusion" is that it "determined" that a change "was unjustified." 587 U.S. at 324 (Alito, J., concurring in judgment). To presume instead that the FDA rejected a scientifically *justified* warning for superficial or easily fixable reasons "overlook[s] the FDA's *raison d'etre*" to protect the public health. Pet.App.150a. It also overlooks FDA regulations: As the agency told this Court last time, it does not reject substantiated warnings based on "editorial" objections; it instead conditions approval on "changes" to the proposed labeling. 21 C.F.R. § 314.105(b); *id.* § 314.110(a)(4); C.A.App.1505.

Consistent with Justice Alito's concurrence, Judge Wolfson properly relied on inferences from this legal context to determine the best reading of the CRL—that the FDA "did not believe there was reasonable scientific evidence of a causal association between bisphosphonate use and atypical femoral fractures" in 2008. Pet.App.152a. If the words "stress fracture" had been "the sole problem with [the] 2008 warning, then the FDA could have simply stricken it, as it did two years later, or approved it on the condition" that Merck edit the wording. Pet.App.152a-153a. That is exactly what the FDA did *elsewhere in the CRL itself*, by revising Merck's proposed changes to the Adverse Reactions section. C.A.App.1153.

2. The Third Circuit once again rejected the entire project. Tellingly, it reached its (non)decision on the meaning of the CRL *before* considering any of this legal context. Then, when purporting to consider the concurrence's point, the panel refused to accept the clear inference: that, in denying Merck's proposal and declining to offer any alternative, the FDA necessarily determined that the scientific data did not yet show a causal relationship sufficient to support a warning. Instead, the court stretched to find reasons to ignore that implication. For the first time, the Third Circuit saw fit to consult "informal FDA communications"—the same evidence it had refused to consider when interpreting the CRL—but only to deem legal context *irrelevant*. Pet.App.71a-73a.

The Third Circuit was so determined to ignore the "governing … context," *Albrecht*, 587 U.S. at 316, that it contradicted its *own interpretation* of the CRL. Mere pages before, it held that the "presumption" required it to adopt the CRL's sole *non*-preemptive reading—*i.e.*, that the FDA wanted to warn about the fracture risk, but disliked Merck's wording and therefore said no and moved on. That view cannot be squared with the FDA's statutory duty or with its own regulations. So the Third Circuit pivoted, citing extrinsic evidence that the FDA was "still assessing evidence" and "not fully convinced of the link" between Fosamax and atypical femoral fractures in 2008. Pet.App.71a.

That analysis (while a few pages too late) is *correct*: The record *does* show that the agency was unconvinced that the risk raised by Merck bore the requisite causal connection to bisphosphonate use—and that it was not so convinced until the 2010 Task Force report. But the Third Circuit failed to appreciate the legal effect of

that fact: Until the new evidence emerged in late 2010, the FDA would not have blessed *any* warning about atypical fractures. Under *Albrecht*, that preempts. *See* 587 U.S. at 303. Indeed, this is the very definition of impossibility preemption.

The bottom line is that Justice Alito's insight neatly solves every case like this one. If the manufacturer informs the FDA about a risk and proposes a warning, and the FDA denies the proposal without directing an alternative—that establishes impossibility, without any need to dig into extrinsic evidence. Yet, for courts in the Third Circuit trying to interpret the meaning of FDA actions, *legal* context is just as off-limits as *factual* context—the only acceptable outcome is for the defendant to lose.

3. No other court has treated the legal context for FDA action as irrelevant to the preemption inquiry. *Cf. Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1103 (10th Cir. 2017) (holding that preemption cannot be rejected "based on speculation that the FDA would jettison its legal requirements"). Instead, courts have properly accounted for § 355(*o*) and FDA silence.

For instance, the district court in the Zofran MDL found state-law tort claims preempted based in part on inferences from the legal context. *See In re Zofran (Ondansetron) Prods. Liab. Litig.*, 541 F. Supp. 3d 164, 194, 202 (D. Mass. 2021), *aff'd*, 57 F.4th 327 (1st Cir. 2023). The court reasoned that "[a]ccepting [the] plaintiffs'" account of the record "would suggest that the FDA … turned a blind eye to evidence that Zofran causes birth defects." *Id.* But the court found it "highly unlikely" that "the FDA intended to leave open the possibility that enhanced pregnancy warnings

would be appropriate in a different section of the label," but then "refused to take up the issue with [the manufacturer] based on the technical point that [it] had not sought to change that specific section." *Id.* (citing *Cerveny*, 855 F.3d at 1103). That is the precise logic that the Third Circuit refused to follow.

Similarly, the Southern District of California found the FDA's "authority to mandate a label change if it learns of new safety information … highly relevant" to preemption. *In re Incretin-Based Therapies*, 524 F. Supp. 3d at 1032. The court could not "simply ignore" evidence of the FDA's "commitment to actively and continuously monitoring" a possible link between the drug and the relevant risk. *Id.* at 1033. Given that context, the FDA's "silence" supported a finding of preemption. *Id.* at 1032; *accord Ridings*, 444 F. Supp. 3d at 998 (relying on FDA's failure to "take[] any action to substantively alter Pradaxa's warning"). The Third Circuit refused, however, to draw this same inference.

* * *

In *Albrecht*, this Court adopted a clear test for when FDA labeling rules preempt state liability. Instead of applying that test, the Third Circuit developed a way to avoid it—pretermitting the inquiry into extrinsic evidence and mangling the inquiry into legal context. The consequence of this outlier approach is that Merck now faces sweeping liability even though two district judges *and the FDA itself* have recognized that federal law prohibited the warning Respondents say was needed—and even though the court below *did not find otherwise*. This Court should not let this deeply flawed and manifestly unfair decision stand.

II. THE THIRD CIRCUIT'S APPROACH PUTS DRUG MANUFACTURERS IN AN IMPOSSIBLE POSITION.

Left in place, the Third Circuit's decision to load the evidentiary dice in favor of plaintiffs will render it virtually impossible for manufacturers to comply with the federal labeling regime while avoiding state tort liability. That is bad for manufacturers and patients alike. This Court should correct the Third Circuit's errors before they undermine the FDA's cooperative regulatory process, increase drug costs, or trigger a flood of counterproductive overwarning.

This Court has repeatedly granted certiorari in this area, even in the absence of a sharp circuit split, due to the "importance of the pre-emption issue" to the pharmaceutical industry. *Wyeth*, 555 U.S. at 563; *see also* Pet. for a Writ of Cert. in *Albrecht*, 2017 WL 3701808, at *30-*33; Pet. for a Writ of Cert. in *Mensing*, 2010 WL 638478, at *19-*25; Pet. for a Writ of Cert. in *Wyeth*, 2007 WL 776723, at *13-*15. As the FDA explained when last urging this Court to grant review, the "practical implications" of improperly narrowing preemption "are starkly illustrated by the volume of tort claims asserted against [Merck]." C.A.App.1506. Without federal guardrails, state tort liability risks "whipsawing the medical community," *Wyeth*, 555 U.S. at 626 (Alito, J., dissenting), and thus jeopardizes access to safe and affordable medicines by "rais[ing] prices to the point where those who are sick are unable to obtain the drugs they need," *id.* at 582 (Breyer, J., concurring). And in the Third Circuit, the stakes of error are especially high: New Jersey is home to many of the world's largest pharmaceutical companies, including Merck.

The decision below implicates these concerns by stripping drug manufacturers of a preemption defense whenever the FDA's labeling judgments could be seen as facially ambiguous. Assuming a plaintiff can offer a colorable non-preemptive gloss on a CRL or similar action, the court is barred from even *trying* to resolve that ambiguity—either by consulting record evidence bearing on the agency's meaning or by drawing the legal inference that Justice Alito identified.

And, make no mistake: There will always be enough ambiguity for creative plaintiffs' lawyers to exploit with the benefit of hindsight. CRLs are concise, non-public documents directed solely to the manufacturer, and thus presume familiarity with the parties' previous communications and the regulatory context. The one here is illustrative. The factual record and legal context confirm that the agency would not have approved an atypical fracture warning before 2010. The FDA *itself* represented as much to this Court. All of the extrinsic evidence pointed powerfully in that direction, to the point that the district court called it "clear and convincing." Pet.App.79a. Nevertheless, the fact that the agency scientist who drafted the CRL used language *susceptible* to a different interpretation was enough to impose massive potential liability.

Merck would welcome a world in which every CRL is unambiguous. But manufacturers have no control over FDA drafting choices—they must do their best to comply with federal and state law based on the orders they receive. And in the Third Circuit, a manufacturer who receives any arguably ambiguous FDA denial faces a stark choice.

The first option is to treat the denial as based on the science, stand down—and invite years of expensive, high-risk mass-tort litigation. The second is to presume the FDA rejected the proposal based on a quibble over wording or placement, while ignoring its duty to address the issue and the regulatory context. The manufacturer would then inundate the FDA with new proposals, clarification requests, and attempts to smoke out its true grounds. Those efforts could trigger an enforcement action, and would surely undermine the manufacturer's most vital regulatory relationship.

It would also hinder the FDA's mission. This Court has warned against liability rules that give regulated parties "an incentive to submit a deluge of information that the [FDA] neither wants nor needs." *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 351 (2001). That is especially important in the context of a regime "designed to 'prevent overwarning'" though "'[e]xaggeration of risk, or inclusion of speculative or hypothetical risks,' that 'could discourage appropriate use of a beneficial drug.'" *Albrecht*, 587 U.S. at 304. Worse, the Third Circuit's "presumption" guarantees that, even where the FDA *did* intend to *prohibit* a manufacturer from warning of a risk, it can still face liability for *failing* to warn of it. That delegates power from an expert agency to the plaintiffs' bar by forcing courts to reverse the agency's policy judgment as soon as a plaintiff identifies an ambiguity.

There is zero basis in law, policy, or basic fairness to impose the Third Circuit's Catch-22. Its decision creates an untenable situation for pharmaceutical manufacturers—and, by extension, for the millions of patients who rely on them. This Court should again grant review, and reverse.

CONCLUSION

This Court should grant the petition.

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Respectfully submitted,

STEPHEN E. MARSHALL
VENABLE LLP
750 East Pratt St.
Baltimore, MD 21202

NOEL J. FRANCISCO
Counsel of Record
JEFFREY R. JOHNSON
JOHN HENRY THOMPSON
JONES DAY
51 Louisiana Ave., NW
Washington, DC 20001
(202) 879-3939
nfrancisco@jonesday.com

JOHN R. BOULÉ III
JONES DAY
555 South Flower St.
Fiftieth Floor
Los Angeles, CA 90071

Counsel for Petitioner