UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: XARELTO (RIVAROXABAN) PRODUCTS LIABILITY LITIGATION	**MDL No. 2592** **SECTION L**
THIS DOCUMENT RELATES TO:	**JUDGE ELDON E. FALLON**
Harriet Ibanez, et al. v. Janssen Research & Development, LLC f/k/a Johnson & Johnson Pharmaceutical Research & Development, LLC, et al. **Case No. 2:14-cv-02669**	**MAGISTRATE NORTH**

MEMORANDUM IN SUPPORT OF DEFENDANTS' JOINT MOTION TO CERTIFY FOR INTERLOCUTORY APPEAL UNDER 28 U.S.C. § 1292(b)

Defendants have moved for summary judgment on Plaintiffs' failure-to-warn and design-defect claims on the grounds that they are preempted by federal law. Docs. 7653, 7660. The Court should grant those motions for the reasons set forth in Defendants' briefing. But if the Court adheres to its prior rulings rejecting preemption, the Court should certify its order for immediate interlocutory appeal under 28 U.S.C. § 1292(b).

This litigation is ripe for appellate review. Now that three bellwether trials have resulted in defense verdicts, judicial economy necessitates that the parties receive guidance from the Fifth Circuit as to whether the defense of federal preemption can dispose of many or all of the claims in this MDL without having to try more than 20,000 cases. The Fifth Circuit has held that "[w]hether federal law preempts [a plaintiff's] claims certainly falls within the ambit of 28 U.S.C. § 1292(b)." *Spong v. Fid. Nat. Prop. & Cas. Ins. Co.*, 787 F.3d 296, 304 (5th Cir. 2015) (holding that court had jurisdiction to hear interlocutory appeal of preemption ruling). That is certainly true here.

The use of § 1292(b) to review Defendants' preemption defenses is critical. The pivotal preemption issues presented in Defendants' pending motions have divided the lower federal courts, including in cases involving other medications in the same class as Xarelto facing similar liability

claims. Indeed, the MDL court overseeing litigation involving failure-to-warn and design-defect claims arising out of the plaintiffs' use of Eliquis (another novel oral anticoagulant in the same class as Xarelto) held those claims preempted. *See Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166 (S.D.N.Y. 2016) ("*Utts I*"); *Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644 (S.D.N.Y. 2017) ("*Utts II*"). And an immediate appeal will "materially advance the ultimate termination of the litigation" by providing vital legal guidance, regardless of how the Fifth Circuit rules.

Certification under § 1292(b), moreover, is the only path to appellate review of these critical issues within a reasonable timeframe. Three bellwether trials in this MDL have resulted in unanimous defense verdicts after denial of Defendants' preemption motions. The fourth scheduled bellwether trial was dismissed with prejudice while Defendants' preemption motions were pending, after the case had been fully worked up for trial. Defendants intend to raise federal preemption as an alternative ground for affirmance in the pending consolidated appeal from the first three bellwether trials, but the Fifth Circuit is not required to consider an alternative ground for affirmance, and is unlikely to do so, unless in the unlikely event it finds reversible error in this Court's evidentiary rulings or jury instructions. This pattern is not limited to this MDL—in the first two Xarelto bellwether trials in the Pennsylvania Court of Common Pleas, rulings rejecting Defendants' preemption arguments again have been followed by a jury verdict or a judgment in Defendants' favor on other grounds.

The Court knows firsthand the enormous time and effort required to prepare and try each of these cases. That burden falls not only on the parties, but also on the judicial system itself. And that burden will increase exponentially when the approximately 1,200 cases selected for pretrial workup under CMO 6 are remanded to federal judges throughout the country without appellate

guidance on preemption. Certification here thus may avoid or curtail a "'long and costly process of serial trials.'" *In re Chinese-Manufactured Drywall Prods. Liab. Litig.*, No. 2:09-md-2047, Doc. 20890, at 12 (E.D. La. Aug. 4, 2017) (Fallon, J.) (quoting *Lester v. Exxon Mobil Corp.*, No. 14-cv-1824, 2014 WL 5393506, at *6 (E.D. La. Oct. 23, 2014), *aff'd*, 879 F.3d 582 (5th Cir. 2018)).[1]

In short, this Court's ruling on Defendants' preemption motions is precisely the kind of order for which certification under § 1292(b) was designed. Congress "adopted [§ 1292(b)] with complex litigation in mind," MANUAL FOR COMPLEX LITIGATION (4th Ed.) § 15.11, and the Federal Judicial Center's Manual for Complex Litigation notes that "orders . . . granting or denying motions disposing of pivotal claims or defenses" are among the "crucial orders" that are well-suited for interlocutory appeal under this provision, *id.* The Manual also emphasizes that a mass tort case is not "mature" until "appellate review of novel issues has been completed." *Id.* § 22.314. Certification is amply warranted here.

PROCEDURAL HISTORY

In the first three bellwether trials in this MDL—*Boudreaux*, *Orr*, and *Mingo*—this Court denied Defendants' motions for partial summary judgment on preemption. *See* Docs. 6196, 7110. In so doing, the Court ruled on Defendants' labeling preemption motion that anecdotal reports of adverse events about bleeding—a known side effect of any anticoagulant, which Xarelto's labeling warns of repeatedly—can constitute "newly acquired information" under FDA's "Changes Being Effected" ("CBE") regulation, 21 C.F.R. § 314.70(c)(6)(iii) that would have permitted Defendants to change the Xarelto label. The Court also ruled that there was no "clear evidence," *Wyeth v.*

[1] The Court temporarily vacated and then reinstated its certification order in *Chinese Drywall* after an intervening Supreme Court decision.

Levine, 555 U.S. 555, 571 (2009), that FDA would have rejected a Neoplastin PT instruction in Xarelto's labeling, even though Janssen proposed—and FDA struck—similar language during the pre-market approval process. The Court likewise found no "clear evidence" that FDA would have rejected warnings about U.S. subgroup data or about a recall of the INRatio device used during clinical testing, even though FDA rejected warnings about those topics as well. And the Court also ruled on Defendants' design preemption motion that federal law does not preempt a claim that Defendants should have designed Xarelto differently from the outset, even though federal law prohibited Defendants from selling any alternative design without FDA's prior approval. In all three bellwether trials, the jury returned a unanimous verdict in Defendants' favor. Plaintiffs' consolidated appeal from those three defense verdicts is now pending before the Fifth Circuit. *In re Xarelto Prods. Liab. Litig.*, No. 17-30845 (5th Cir.).

Defendants then moved for summary judgment on preemption grounds in the fourth scheduled bellwether trial, *Henry*, as well as in *Ibanez*, a case included in the discovery pool by random selection of the Court. Docs. 7653, 7660. The plaintiff in *Henry* moved to voluntarily dismiss his complaint with prejudice, which the Court allowed, rendering Defendants' preemption motions in that case moot. *See* Docs. 7816, 7943. In *Ibanez*, however, Plaintiffs opposed Defendants' preemption motions, in part on the ground that incomplete discovery prevented Plaintiffs from "present[ing] facts essential to justify [their] opposition" under Federal Rule of Civil Procedure 54(d). *See* Doc. 7962. The discovery issues were resolved, in part by the parties themselves and in part by the Court, *see* Doc. 9211, after which Plaintiffs filed a supplemental opposition to the labeling-preemption motion, *see* Doc. 9594. Defendants are filing their replies in support of their preemption motions concurrently with this Motion. The Court has agreed to hear argument on this certification motion after the June 27, 2018, case management conference.

LEGAL STANDARD

By statute, an appeal of an interlocutory order is permitted when the district court "shall be of the opinion [1] that such order involves a controlling question of law [2] as to which there is substantial ground for difference of opinion and [3] that an immediate appeal from the order may materially advance the ultimate termination of the litigation," and when the court "so state[s] in writing in such order." 28 U.S.C. § 1292(b). If the district court certifies its order, the appropriate court of appeals "may thereupon, in its discretion, permit an appeal to be taken from such order." *Id.* Issues of federal preemption are a common subject of interlocutory appeals under this provision. *See, e.g.*, *Spong*, 787 F.3d at 304; *Greenwich Ins. Co. v. Miss. Windstorm Underwriting Ass'n*, 808 F.3d 652, 655 (5th Cir. 2015) (deciding § 1292(b) interlocutory appeal of preemption ruling); *see also* MANUAL FOR COMPLEX LITIGATION (4th ed.) § 15.11.

REASONS CERTIFICATION SHOULD BE GRANTED

This case involves important and controlling legal questions about whether federal law preempts state-law failure-to-warn and design-defect claims regarding a medication whose labeling and design FDA has repeatedly approved as "safe and effective"—without the warnings or design modifications Plaintiffs advocate. If this Court denies Defendants' preemption motions, the Court's order will easily satisfy each of the three requirements for certification under § 1292(b). Indeed, the Fifth Circuit has recognized that "[w]hether federal law preempts [a plaintiff's] claims certainly falls within the ambit of 28 U.S.C. § 1292(b)." *Spong*, 787 F.3d at 304. This is a paradigmatic case for certification under that provision.

I. The Court's Preemption Ruling Will Resolve Controlling Questions of Law.

If this Court denies Defendants' pending motions, the Court's resulting order will resolve "controlling question[s] of law"—in particular, whether federal law preempts Plaintiffs' state-law failure-to-warn and design-defect claims.[2]

To begin with, federal preemption is a "question of law," 28 U.S.C. § 1292(b), as this Court has recognized. *See, e.g.*, Doc. 6254, at 5. That legal question also is "controlling." A question is "controlling" for purposes of § 1292(b) where "its incorrect disposition would require reversal of a final judgment." WRIGHT & MILLER, FEDERAL PRACTICE & PROCEDURE § 3930. That is indisputably the case here—if this Court finds that Plaintiffs' claims are not preempted, Plaintiffs prevail on those claims at trial, and the Fifth Circuit later concludes that the claims *are* preempted, the Fifth Circuit would have no choice but to reverse. For that reason, the Fifth Circuit has observed that the question of federal preemption "certainly" satisfies the "controlling question of law" element of § 1292(b). *Spong*, 787 F.3d at 304.

A question also is controlling if its resolution on interlocutory review "might save time for the district court, and time and expense for the litigants." WRIGHT & MILLER, FEDERAL PRACTICE & PROCEDURE § 3930; *see also Chinese-Manufactured Drywall*, No. 2:09-md-2047, Doc. 20890 at 12 (certifying question to avoid a "long and costly process of serial trials" (quotation marks omitted)). That too is the case here, since an appellate ruling on preemption in this case would control the preemption analysis for the many thousands of cases pending in this MDL. The Fifth Circuit's ruling thus will "have precedential value for a large number of cases"—indeed, an

[2] Section 1292(b) provides for district courts to certify an "order" for interlocutory review, not a particular question or questions. *See Castellanos-Contreras v. Decatur Hotels, LLC*, 622 F.3d 393, 398–99 (5th Cir. 2010) (en banc). "[I]n certifying an order for interlocutory review," however, "it is helpful if the district judge frames the controlling question(s) that the judge believes is presented by the order being certified." *Linton v. Shell Oil Co.*, 563 F.3d 556, 557 (5th Cir. 2009).

extraordinarily large number of cases, given the size of this MDL. *In re Delta Produce*, No. BR 12-50073-A998, 2013 WL 3305537, at *2 (W.D. Tex. June 28, 2013). And so resolution of these critical preemption issues would obviate the need for repeated trials on similar claims, easing the burden on the judicial system and the parties.

II. The Court's Preemption Ruling Will Resolve Questions on Which There Is Substantial Ground for Difference of Opinion.

There is "substantial ground for difference of opinion," 28 U.S.C. § 1292(b), on whether federal law preempts Plaintiffs' state-law failure-to-warn and design-defect claims here. Defendants' pending preemption motions implicate several important issues on which the lower federal courts are split, including:

- Whether accumulating adverse event reports regarding a known risk that is disclosed in the medication's labeling can constitute "newly acquired information" under FDA's CBE regulation, 21 C.F.R. § 314.70(c)(6)(iii);
- Whether FDA's decision to strike language from a medication's proposed labeling is "clear evidence," *Levine*, 555 U.S. at 571, that FDA would not have approved a unilateral change adding language to the same effect back into the labeling;
- Whether the Supreme Court's decisions in *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011), and *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013)—which hold that federal law preempts failure-to-warn and design-defect claims if the manufacturer needs FDA's advance approval to make a change—apply to manufacturers of both generic and brand-name medications; and
- Whether federal law preempts so-called "pre-approval" design-defect claims—that is, claims alleging that a manufacturer should have altered a medication's design before seeking initial marketing approval from FDA.

This Court has noted the "divide among federal and state court on the issue of FDA preemption." Doc. 7110, at 7. The Court's preemption ruling will only add to that divide.

A. There is ground for disagreement about whether accumulating adverse event reports about a known risk can constitute "newly acquired information."

As explained in Defendants' preemption motion regarding Plaintiffs' failure-to-warn claims, state-law tort claims against a manufacturer of a prescription medication are preempted unless during the relevant period, the manufacturer possessed "newly acquired information" that "reveal[ed] risks of a different type or greater severity or frequency than previously included in submissions to FDA." 21 C.F.R. § 314.70(c)(6)(iii), 314.3(b); *see* Doc. 7660 at 12, 20–23. Absent such information, federal law prohibits a manufacturer from using the CBE regulation to unilaterally change the medication's labeling to add a new warning, and the manufacturer instead must obtain FDA's prior approval. *See* 21 C.F.R. § 314.70(b)(v), (c)(6)(iii). "The question for 'impossibility' preemption," however, "is whether the private party could *independently*"—that is, "unilaterally"—do under federal law what state law requires of it." *Mensing*, 564 U.S. at 620 (emphasis added); *see also Bartlett*, 133 S. Ct. at 2470. "[W]hen a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for preemption purposes." *Mensing*, 564 U.S. at 623–24. It is the plaintiff's burden, moreover, to identify "newly acquired information" sufficient to justify a unilateral CBE supplement. *See In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34, 41–43 (1st Cir. 2015); *Ideus v. Teva Pharms. USA, Inc.*, No. 4:16-CV-3086, 2017 WL 6389630, at *2–3 (D. Neb. Dec. 12, 2017); *Utts II*, 251 F. Supp. 3d at 661. If Plaintiffs cannot do so here, their state-law failure-to-warn claims are preempted.

In this Court's prior orders denying Defendants' preemption defenses, the Court held that Defendants possessed "newly acquired information" because they "became aware of the number of [their] consumers claiming they experienced a major bleeding event while taking Xarelto." Doc.

6196 at 7–8; Doc. 7110 at 10. In their opposition to Defendants' preemption motions, Plaintiffs also argue that the raw number of serious adverse events reported to FDA after the medication's approval, as well as a report by a third-party watchdog organization (co-authored by one of Plaintiffs' retained experts, who failed to disclose his conflict of interest) summarizing those adverse event reports, would have justified a unilateral CBE supplement.[3] *See, e.g.*, Doc. 7962 at 23–24, 36–38.

Even assuming that these adverse event reports may be "newly acquired," Plaintiffs have not shown that they "reveal[ed] risks of a different type or greater severity or frequency than previously included in [prior] submissions to FDA." 21 C.F.R. § 314.3(b). Defendants submitted clinical studies to FDA before Xarelto's approval showing that the medication presents a risk of serious, and possibly fatal, bleeding—as any anticoagulant inherently does—which is why Xarelto's labeling warns about that risk dozens of times. *See* Doc. 7660 at 1.

Adverse event reports, moreover, are purely anecdotal. They are "voluntarily submitted . . . by consumers and/or members of the health profession" and are "not . . . scientifically or otherwise verified." Doc. 7660-37 at 5 (FDA document describing Adverse Event Reporting System). "For any given report, there is no certainty that the suspected drug caused the reaction," in part "because physicians are encouraged to report *suspected* reactions." *Id.* (emphasis added); *see also* 21 C.F.R. § 314.80(a), (l). And FDA "does not receive reports for every adverse event . . . that occurs with a product" since "[m]any factors can influence whether or not an event will be reported," including "the time a product has been marketed." *Utts*, 251 F. Supp. 3d at 663–64 (quoting FDA website). "Accumulated case reports" thus "cannot be used to calculate incidence or estimates of drug risk." Doc. 7660-37 at 5. As the Supreme Court has observed, "the mere

[3] Mingo Trial Tr. 1093:16–1094:7 (Exh. 1); *see also, e.g.*, ISMP, QuarterWatch Q4 2016 (Exh. 2).

existence of reports of adverse events . . . says nothing in and of itself about whether the drug is causing the adverse events." *Matrixx Initiatives, Inc. v. Siracusano*, 563 U.S. 27, 44 (2011). Indeed, a recent analysis using FDA's new Sentinel monitoring system has confirmed that Xarelto's risk-benefit profile during its first three-and-a-half years on the market was similar, if not superior, to what FDA had anticipated when it first approved the medication in 2011. *See* Elizabeth A. Chrischilles et al., *Prospective Surveillance Pilot of Rivaroxaban Safety Within the US Food and Drug Administration Sentinel System*, 27 PHARMACOEPIDEMIOLOGICAL DRUG SAFETY 263, 268–69 (2018) (Exh. 3).

For precisely this reason, the district court overseeing the MDL for Eliquis—another anticoagulant in the same medication class as Xarelto—held that a third-party Plaintiffs' expert watchdog report drawn from adverse events reported to FDA did not constitute "newly acquired evidence" sufficient to avoid preemption. "The table and the description from the [watchdog] report," the court explained, "do not suggest . . . that the real-world signal data for Eliquis shows a greater severity or frequency of bleeding events or deaths than previously disclosed in Eliquis' submissions to the FDA." *Utts II*, 251 F. Supp. 3d at 665. So too here. In fact, FDA has repeatedly concluded that changes to Xarelto's label based on the accumulation of data about bleeding rates is unwarranted. *See* Defs.' Reply in Support of Labeling Preemption Mot. at 4–5. Nor do adverse event report "bleeding rates" relate to the use of a PT test, data from ROCKET AF, or the recall of the INRatio device. *Id.*

Plaintiffs have attempted to distinguish *Utts*, contending that unlike the watchdog report for Eliquis, the report for Xarelto deemed the accumulating adverse events reports to be an "important safety signal." Doc. 7962 at 39. Plaintiffs also assert that Xarelto had more adverse event reports than warfarin, to which Xarelto was shown to be non-inferior before approval. *Id.*

Those arguments however, are nonresponsive to the fundamentally anecdotal, unreliable, and non-causal nature of adverse event reports. More importantly, even if this Court accepts one or both of Plaintiffs' distinctions, *Utts* at a minimum shows that there is substantial ground for a court to conclude that accumulating adverse event reports about a known risk do not constitute "newly acquired information" under the CBE regulation. And that is all § 1292(b) requires.

B. There is ground for disagreement about whether FDA's deletion of proposed language is "clear evidence" that FDA would reject a labeling change.

Even if a manufacturer possessed "newly acquired information" during the relevant period that would have justified a unilateral labeling change, state-law tort claims still are preempted if there is "clear evidence that the FDA would not have approved" the labeling change that state law requires. *Wyeth*, 555 U.S. at 571; *see* Doc. 7660 at 17–19.

Plaintiffs argue that state law required Defendants to instruct physicians to perform a Neoplastin PT blood test in order to identify patients who may be at an increased risk of bleeding. As explained in Defendants' motion and in numerous trial witnesses' testimony, however, FDA expressly struck PT-related information from Defendants' labeling proposals. *See* Doc. 7660 at 5–11, 19. In its prior orders on preemption, this Court held that FDA's deletions did not provide the requisite "clear evidence" because "there was no indication that the Defendant[s] had 'earnestly attempted' to strengthen the warning or that the FDA had 'specifically disallowed' stronger language." Doc. 6196 at 8 (quoting *Levine*, 555 U.S. at 561). The Court reasoned that "the FDA and defendants are required to give more than 'passing attention' to the issue—there must be evidence the FDA intended or would *prohibit* a defendant from strengthening [the] warning." *Id.*; *see also* Doc. 7110 at 11–12. Plaintiffs reiterate these arguments in their initial and supplemental oppositions, contending that Defendants failed to adequately press FDA after the agency's initial rejections of Defendants' proposed PT-related language. *See* Doc. 7962 at 39–44; Doc. 9594 at 6.

In a similar vein, Plaintiffs also argue that state law required Defendants to warn about data collected from the U.S. subgroup of the ROCKET AF clinical trial. But again, FDA expressly struck proposed labeling that would have warned that "North American subjects on XARELTO experienced a higher annual bleeding rate compared to their warfarin treated counterparts than subjects from any other region." Doc. 7660-42 at 24. In its prior order, this Court found this evidence less than "clear" because "Defendants did not push the FDA on the issue, and the FDA later added the information sua sponte." Doc. 7110 at 11.[4]

Plaintiffs cite only two cases where other courts have rejected a preemption defense on the ground that the manufacturer failed to press FDA after an initial rejection. *See In re Fosamax (Alendronate Sodium) Prod. Liab. Litig.*, 852 F.3d 268, 290–91, 299 (3d Cir. 2017), *pet'n for cert. pending*, No. 17-290 (U.S.); *Aaron v. Wyeth*, No. 2:07CV927, 2010 WL 653984, at *6 (W.D. Pa. Feb. 19, 2010). Both of those cases are distinguishable. In *Fosamax*, the Third Circuit held that "clear evidence" preemption under *Levine* is a question of fact for a jury, not a question of law for the court, as this Court has held. *See* 852 F.3d at 293; Doc. 6254 at 5.[5] And in *Aaron*, the manufacturer did not provide warnings specific to its own medication, and instead "acquiesced to" standardized "class labeling" for the entire category of medications. 2010 WL 653984, at *6.

[4] Plaintiffs also argue that state law required Defendants to provide a warning about a recall of the INRatio device used to monitor patients on warfarin in ROCKET AF. Doc. 7962 at 47–49. Although FDA did not strike proposed language about this warning, FDA expressly told Defendants, after investigating the INRatio issue, that "no changes in rivaroxaban labeling to reflect the impact of use of the INRatio device in ROCKET are warranted." Doc. 7660-40 at 5. Whether an explicit FDA decision not to change the label satisfies the clear-evidence standard raises the same issue as the Agency's strikethrough decisions and also should be resolved on interlocutory appeal.

[5] The Solicitor General recently submitted a brief to the Supreme Court urging the Supreme Court to grant the petition for certiorari filed by name-brand manufacturer Merck seeking review of *Fosamax*. *See* Br. for the United States as Amicus Curiae, *Merck Sharp & Dohme Corp. v. Albrecht*, No. 17-290 (U.S., filed May 23, 2018). The Solicitor General's brief argues that the Third Circuit in *Fosamax* erred in holding that preemption under *Levine* presents a factual question for a jury. *Id.* at 12–19. (Again, this Court has held that preemption is a legal question for the court. *See* Doc. 6254 at 5.) The Solicitor General's brief also argues, consistent with Defendants' arguments in their preemption motion here, that because FDA rejected a proposal by Merck to add a warning about a particular type of injury, federal law preempts state-law failure-to-warn claims arising from that same type of injury. *Id.* at 12, 19–22.

On the other side of the ledger, numerous courts—including at least two courts of appeals—have held that a manufacturer satisfies *Levine*'s "clear evidence" requirement if it shows that FDA rejected a proposed warning that is substantially similar to that required by state law.[6] This is true even if the manufacturer never proposed a different warning. The Tenth Circuit, for example, described an FDA rejection of a third-party citizen's petition as not just "clear evidence," but a "smoking gun." *Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1103 n.11 (10th Cir. 2017). Even if this Court finds that decision and the many others like it unpersuasive or distinguishable in some way, they plainly provide ample ground for fair-minded jurists to disagree about Defendants' preemption defense. And again, that is all § 1292(b) requires.[7]

C. There is ground for disagreement on whether federal law preempts Plaintiffs' design-defect claims.

There also is substantial ground for disagreement on whether federal law preempts Plaintiffs' design-defect claims. In its earlier orders, this Court held that federal law does not

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[6] *See Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1105 (10th Cir. 2017) (FDA's rejection of a citizen petition that presented "claims and data virtually identical to those submitted by" the plaintiffs "constitutes clear evidence"); *Christison v. Biogen Idec Inc.*, 199 F. Supp. 3d 1315, 1346-48 (D. Utah 2016) (clear evidence where FDA twice rejected proposed labeling changes to warn about the risk); *Rheinfrank v. Abbott Labs.*, 119 F. Supp. 3d 749, 766 (S.D. Ohio 2015), *aff'd*, 680 F. App'x 369, 385 (6th Cir. 2017) ("[B]ecause the evidence in the record reveals that the FDA twice rejected Abbott's attempts to strengthen Depakote's label to add a developmental delay warning, there was clear enough evidence under Wyeth that the FDA would not have approved any such change …."); *In re Depakote*, 87 F. Supp. 3d 916, 922 (S.D. Ill. 2015) (clear evidence where "Abbott tried, on various occasions, to secure approval of a developmental delay warning, and its requests were twice denied by the FDA"); *Dobbs v. Wyeth Pharm.*, 797 F. Supp. 2d 1264, 1274–75 (W.D. Okla. 2011) ("[T]his court does not interpret Levine as imposing upon the drug manufacturer a duty to continually 'press' an enhanced warning which has been rejected by the FDA."); *see also Newman v. McNeil Consumer Healthcare*, No. 10-CV-01541, 2012 WL 39793, at *7–8 & n.8 (N.D. Ill. Jan. 9, 2012) (rejecting preemption defense but noting that FDA need not "reject every possible formulation of a particular warning in order for there to be clear evidence").

[7] As Defendants' labeling-preemption motion explains, Plaintiffs' PT-related failure-to-warn claims are preempted for two additional independent reasons. First, FDA regulations prohibited Defendants from unilaterally changing Xarelto's labeling to recommend an unapproved, "off-label" use of the Neoplastin PT test. *See* Doc. 7660 at 14–17. Second, Plaintiffs' desired PT-related warning is a "monitoring recommendation" that must appear in the "Highlights" section of the labeling, which FDA regulations barred Defendants from changing unilaterally. *Id.* at 23–25. Because these additional arguments are well-supported by FDA's regulations and the Supreme Court's preemption jurisprudence, there is substantial ground for difference of opinion about them. *See Chinese-Manufactured Drywall*, No. 2:09-md-2047, Doc. 20890 at 12 (noting that "[v]ery few United States Courts, including in this circuit," had addressed the certified question).

preempt Plaintiffs' "pre-approval" claim that "Defendants should have designed a[] specific assay and/or antidote before sending Xarelto to the FDA for approval." Doc. 6196 at 7; *see* Doc. 7110 at 12. Plaintiffs' opposition makes the same argument, asserting that although "Defendants would have had to get FDA approval in order to market these alternative designs, . . . courts may not presume . . . that the necessary approval would have been denied." Doc. 7954 at 3.

But the Supreme Court's decisions in *Mensing* and *Bartlett* make clear that the relevant question is not whether Defendants could have persuaded FDA to allow Defendants to comply with state law, but whether Defendants "could independently"—that is, "unilaterally"—"do under federal law what state law requires," without even *seeking* FDA's prior permission. *Mensing*, 564 U.S. at 620; *see Bartlett*, 133 S. Ct. at 2470. Critically, Plaintiffs' position here is that state law required Defendants not just to *conceptualize* an alternative design for Xarelto, but to actually *sell* an alternative design in place of Xarelto's present design. *See* Doc. 7954 at 12–13. As Plaintiffs concede, and *Bartlett* makes clear, however, federal law prohibited Defendants from selling any alternative design without seeking and obtaining FDA's prior approval. *See id.*; *Bartlett*, 133 S. Ct. at 2479.

This Court's earlier orders distinguished *Mensing* and *Bartlett* on the ground that they "relate to generic drug manufacturers[,] who are more limited in their ability to make changes to their labels than are manufacturers of name-brand drugs such as Xarelto." Doc. 6196 at 5; *see* Doc. 7110 at 9. A few other courts have drawn that distinction,[8] but many more courts have rejected it.[9] Even if this distinction between brand and generic manufacturers were valid,

[8] *See In re Tylenol (Acetaminophen) Mktg.*, No. 2436, 2015 WL 7075949, at *21 (E.D. Pa. Nov. 13, 2015); *Sullivan v. Aventis, Inc.*, No. 14-CV-2939-NSR, 2015 WL 4879112, at *6 (S.D.N.Y. Aug. 13, 2015); *Estate of Cassel v. Alza Corp.*, No. 12-CV-771-WMC, 2014 WL 856023, at *5 (W.D. Wis. Mar. 5, 2014).

[9] *See, e.g.*, *Hunt v. McNeil Consumer Healthcare*, 6 F. Supp. 3d 694, 702–03 (E.D. La. 2014); *Yates v. Ortho-McNeil-Janssen*, 808 F.3d 281, 293 (6th Cir. 2015); *In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34 (1st Cir. 2015); *Utts I*, 226 F. Supp. 3d 166; *Brazil v. Janssen Research & Dev. LLC*, Civ. A. No. 4:15-CV-0204, 196 F.

moreover, it is irrelevant to Plaintiffs' design-defect claims. Although FDA regulations allow brand-name manufacturers (but not generics) to unilaterally change their *labeling* in some circumstances, the regulations prohibit both brands and generics alike from unilaterally changing a medication's *design* in the way Plaintiffs advocate here. *See* 21 C.F.R. § 310.3(h); *Bartlett*, 133 S. Ct. at 2475, 2479.

Regardless, courts also are split on whether federal law preempts pre-approval state-law design-defect claims like those Plaintiffs assert here. This Court previously relied on *Guidry v. Janssen Pharmaceuticals, Inc.*, 206 F. Supp. 3d 1187 (E.D. La. 2016), which denied a Rule 12(b)(6) motion at the beginning of the litigation and allowed such a claim to proceed notwithstanding a preemption defense, and Plaintiffs' opposition cites three additional cases reaching a similar conclusion.[10] As this Court has recognized, however, a number of courts have come out the other way.[11] Most notably, the Sixth Circuit—the *only* court of appeals to have

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Supp. 3d 1351 (N.D. Ga. 2016); *Fleming v. Janssen Pharm., Inc.*, 186 F. Supp. 3d 826 (W.D. Tenn. 2016); *Barcal v. EMD Serono, Inc.*, No. 5:14-cv-01709, 2016 WL 1086028, at *3–5 (N.D. Ala. Mar. 21, 2016); *Batoh v. McNeil-PPC, Inc.*, 167 F. Supp. 3d 296 (D. Conn. 2016); *Rheinfrank v. Abbott Labs., Inc.*, 137 F. Supp. 3d 1035, 1041 (S.D. Ohio 2015); *Booker v. Johnson & Johnson*, 54 F. Supp. 3d 868, 873 (N.D. Ohio 2014); *Thompson v. Allergan USA, Inc.*, 993 F. Supp. 2d 1007, 1011 (E.D. Mo. 2014); *see also Sikkelee v. Precision Airmotive Corp.*, 822 F.3d 680, 703 (3d Cir. 2016) (applying *Mensing* and *Bartlett* to aviation claims, outside pharmaceutical context altogether); *In re Darvocet, Darvon, & Propoxyphene Prods. Liab. Litig.*, 756 F.3d 917 (6th Cir. 2014) (applying *Bartlett* to former brand-name manufacturers); *Amos v. Biogen Idec Inc.*, 28 F. Supp. 3d 164, 169 (W.D.N.Y. 2014) (holding that federal law preempts design-defect claim asserted against manufacturer of a biologic). *See also In re Vioxx Prod. Liab. Litig.*, MDL No. 1657, 2015 WL 1909859, at *10 (E.D. La. Apr. 21, 2015) (Fallon, J.) ("[T]he scope of the Bartlett holding has been the subject of much debate among lower courts. Some courts read *Bartlett* narrowly to apply only to generic drugs. Others disagree, finding that *Bartlett* preempts design-defect claims against brand-name manufacturers as well." (citations omitted)).

[10] *See Estate of Cassel v. Alza Corp.*, No. 12-CV-771-WMC, 2014 WL 856023, at *6 (W.D. Wis. Mar. 5, 2014); *Young v. Bristol-Myers Squibb Co.*, No. 4:16-CV-00108(DMB)(JMV), 2017 WL 706320, at *8 (N.D. Miss. Feb. 22, 2017); *Trahan v. Sandoz, Inc.*, No. 3:13-CV-350-J-34MCR, 2015 WL 2365502, at *6 (M.D. Fla. Mar. 26, 2015). Plaintiffs also cite two other cases holding design-defect claims not preempted, but where the plaintiffs (unlike Plaintiffs here) did not limit themselves to allegations that the manufacturer should have redesigned the medication pre-approval. *See Warren v. Boehringer Ingelheim Pharm. Inc.*, No. 1:16-CV-01326(SEB)(DML), 2017 WL 3970666, at *15 (S.D. Ind. Sept. 8, 2017); *Tylenol*, 2015 WL 7075949, at *21–22.

[11] *See Yates v. Ortho-McNeil-Janssen*, 808 F.3d 281 (6th Cir. 2015); *Utts I*, 226 F. Supp. 3d at 185–86; *Brazil*, 196 F. Supp. 3d at 1363 ("Any claim by Plaintiff that Defendants should change the formulation of Invokana is preempted by FDA regulations."); *Gustavesen v. Alcon Labs., Inc.*, 272 F. Supp. 3d 241, 255 (D. Mass. 2017) (quoting 21 U.S.C. § 355(a)), *appeal filed*, No. 17-2066 (1st Cir. Oct. 27, 2017); *Chambers v. Boehringer Ingelheim Pharms., Inc.*, No. 4:15-cv-00068, 2018 WL 849081, at *12–13 (M.D. Ga. Jan. 2, 2018); Doc. 7110 at 6–7 (citing *Yates* and *Utts*); *cf.*

addressed this issue—explained that pre-approval design-defect claims necessarily rest on "speculat[ion] that had defendants designed [the product] differently, the FDA would have approved the alternate design." *Yates*, 808 F.3d at 299. Because the manufacturer "could not have complied with whatever pre-approval duty might exist without ultimately seeking the FDA's approval prior to marketing," the court held, any pre-approval design-defect claim was preempted. *Id.* at 300. This Court may continue to disagree with that reasoning, but plainly there are substantial grounds for a difference of opinion. And notably *Yates*, as here, emanated from a large MDL after the completion of general discovery of the defendants.

III. An Immediate Appeal Will Materially Advance the Termination of this Litigation.

Finally, certifying the Court's preemption ruling will "materially advance the ultimate termination of the litigation." 28 U.S.C. § 1292(b). This requirement "is closely tied to the requirement that the order involve a controlling question of law." WRIGHT & MILLER, FEDERAL PRACTICE & PROCEDURE § 3930. "In determining whether certification will materially advance the ultimate termination of the litigation, the district court considers whether it will eliminate the need for trial, eliminate complex issues, or streamline issues to simplify discovery." *In re Stewart*, Civ. Action No. 09-3232, 2009 WL 2461675, at *2 (E.D. La. Aug. 7, 2009) (citation and quotation marks omitted). Here, if Defendants prevail before the Fifth Circuit on any of the issues presented in their pending preemption motions, the resulting decision would eliminate, or at least substantially narrow, some or all of Plaintiffs' pending claims. If some claims remain, the Fifth Circuit's decision still "would affect the scope of the evidence in a complex case, even short of requiring complete dismissal." *Garner v. Wolfinbarger*, 430 F.2d 1093, 1097 (5th Cir. 1970)

Mitchell v. Boehringer Ingelheim Pharms., Inc., 2017 WL 5617473, at *4 (W.D. Tenn. Nov. 21, 2017) (failure-to-warn claim alleging that medication was "unreasonably dangerous because of its labeling at the time it was first marketed" is preempted).

(quotation marks omitted). Beyond the *Ibanez* case, moreover, a reversal in whole or in part would substantially streamline discovery, motions practice, and trials in thousands of other cases in this MDL. And even if the Fifth Circuit affirms, the resulting decision would provide clarity on the governing law and obviate the need for duplicative preemption motions in every case.

In the pending consolidated appeal from first three bellwether trials in this MDL, Defendants intend to raise some (but not all) of the preemption questions at issue here as alternative grounds for affirmance. *See In re Xarelto Prods. Liab. Litig.*, No. 17-30845 (5th Cir.). Because Defendants prevailed in all three bellwether trials, however, the Fifth Circuit may not address those issues in the pending appeal, which principally concerns other issues. Regardless, the pending appeal does not implicate some of Plaintiffs' failure-to-warn theories, because Plaintiffs did not pursue liability theories at trial regarding the U.S. subgroup data or the INRatio recall, and Plaintiffs' opening appellate brief does not mention those theories. And the pending appeal does not implicate design-defect preemption at all—the plaintiffs dismissed their design-defect claims in *Boudreaux* and *Orr* before trial, *see* Docs. 6298, 6601, and they have not appealed the adverse jury verdict on the design-defect claim in *Mingo*. Certification under § 1292(b) thus is the appropriate mechanism—indeed, the only mechanism—to ensure the prompt appellate ruling on federal preemption that the parties and the judicial system sorely need.

CONCLUSION

For the foregoing reasons, if the Court denies Defendants' pending motions for summary judgment on the grounds that federal law preempts Plaintiffs' failure-to-warn and design-defect claims (Docs. 7653 and 7660), the Court should certify its order for an immediate interlocutory appeal under 28 U.S.C. § 1292(b).

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on the 4th day of June, 2018, the foregoing pleading was filed electronically with the Clerk of Court using the CM/ECF system. Notice of this filing will be sent to Liaison Counsel for Plaintiffs by operation of the court's electronic filing system.

/s/ John F. Olinde