Nos. 24-1576(L), 24-1600, 24-1617

UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

AMY BRYANT, M.D.,
Plaintiff-Appellee,
v.
TIMOTHY K. MOORE, *et al.*,
Intervenors/Defendants-Appellants,
and
JOSHUA H. STEIN, in his official capacity
as Attorney General for the State of North Carolina, *et al.*,
Defendants-Appellees.

On Appeal from the United States District Court for the
Middle District of North Carolina, No. 1:23-cv-00077-CCE-LPA

CROSS-APPEAL REPLY BRIEF FOR AMY BRYANT, M.D.

Paul Alessio Mezzina
KING & SPALDING LLP
1700 Pennsylvania Avenue NW
Washington, DC 20006
(202) 737-0500
pmezzina@kslaw.com

Eva A. Temkin
ARNOLD & PORTER KAYE SCHOLER LLP
601 Massachusetts Avenue NW
Washington, DC 20001
(202) 942-5123
Eva.Temkin@arnoldporter.com

Nicole L. Masiello
ARNOLD & PORTER KAYE SCHOLER LLP
250 West 55th Street
New York, NY 10019
(212) 836-7876

Counsel for Amy Bryant, M.D.

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INTRODUCTION

In response to Dr. Bryant's cross-appeal, intervenors make no attempt to defend the reasons the district court gave for upholding some of North Carolina's restrictions on mifepristone. In particular, they do not defend the court's misunderstanding that those restrictions are "unrelated to mifepristone." JA633; *see* Bryant Br. 65–71. Instead, intervenors maintain that states should be free to impose restrictions specific to this REMS drug that FDA has considered and rejected and that obstruct FDA's efforts to assure patient access to the drug. Remarkably, they even suggest (at 16) that the resulting 50-state "patchwork" of conflicting, inconsistent "safety measures" is something courts should celebrate rather than seek to avoid.

That is not the law. While intervenors persist in mischaracterizing Dr. Bryant's arguments to suggest (at 1) they would "radically alter[] the federal-state balance," in truth, it is intervenors' position that would upend that balance. Congress expressly charged FDA with "[a]ssuring access" to REMS drugs and "minimizing burden," especially for "patients who have difficulty accessing health care (such as patients in rural or medical underserved areas)." 21 U.S.C. § 355-1(f)(2). And under

longstanding Supreme Court precedent, a state may not impose restrictions that FDA considered and rejected because they interfere with that "congressionally mandated objective[]." *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 872 (2000).

Even as to non-REMS drugs, no court has ever held that a state can restrict patient access to a drug in ways FDA considered and rejected; and the Supreme Court's decision in *Wyeth v. Levine* strongly suggests that such restrictions are invalid. *See* 555 U.S. 555, 580–81 & n.14 (2009) (emphasizing that FDA "did not consider and reject" the state requirement at issue there). It would be startling for this Court to hold that states are free to second-guess FDA's judgment in this way for REMS drugs, which are subject to particularly intensive federal oversight and access-focused congressional mandates. As intervenors do not dispute, such a holding would apply a fortiori to the many thousands of non-REMS drugs, making its impact even more sweeping.

This Court should accordingly hold that all of the challenged North Carolina restrictions on mifepristone are preempted and reverse the judgment below insofar as it upheld some of those requirements.

ARGUMENT

I. Intervenors mischaracterize Dr. Bryant's argument and the decision below.

At the outset, intervenors' continuing attempts to create confusion about Dr. Bryant's position and the district court's ruling necessitate a brief response. Intervenors put forward a string of internally inconsistent mischaracterizations that ignore Dr. Bryant's arguments and the district court's reasoning.

For example, intervenors state repeatedly, without a single citation, that Dr. Bryant "says that obstacle preemption applies only to state requirements that the FDA has *adopted* and then rejected." Resp./Reply Br. 1 (emphasis added); *see also id.* at 2, 24, 26, 32. That is false. Dr. Bryant has never argued that preemption requires FDA to have adopted a requirement and then rescinded it. Her narrow contention is that a state is preempted from imposing "restrictions that FDA has *considered* and rejected pursuant to the federal REMS statute and that frustrate FDA's efforts to facilitate patient access to the drug." Bryant Br. 7 (emphasis added). *Geier* makes clear that adoption by a federal

agency is not a prerequisite for obstacle preemption. *See* 529 U.S. at 876 ("[A]t no point did [the agency] formally require the use of airbags.").[1]

Elsewhere, intervenors acknowledge that Dr. Bryant challenges restrictions "'FDA explicitly considered and rejected'" but suggest this is an attempt to "narrow" the district court's decision. Resp./Reply Br. 5 (quoting Bryant Br. 6). That, too, is false: The district court embraced the same preemption test advocated by Dr. Bryant. *See, e.g.*, JA615 ("[W]hen a state adopts a law that imposes a requirement a federal agency deliberately rejected because it conflicts with Congress's goals, [the state law] is preempted."); JA628 (a state may not impose "requirements that a federal agency ha[s] affirmatively and clearly rejected as unnecessary or inappropriate"); JA640–641 (states cannot impose restrictions "FDA explicitly considered and rejected … as unnecessary for safe use under

[1] The Attorney General agrees. *See* AG Br. 27 ("[P]reemption principles bar States from imposing restrictions that a federal agency has indisputably considered and rejected in crafting a comprehensive regulatory scheme."). To the extent the Attorney General has pointed out that FDA adopted and rescinded certain restrictions, that only underscores FDA's deliberate rejection of those restrictions. *See* Dkt. 96 at 99 ("[T]he Attorney General's position is not that a requirement must have been imposed and then withdrawn for something to be preempted. It is simply that where a requirement has been imposed and then withdrawn, it becomes an easy case; preemption becomes obvious.").

the statutory regime imposed and required by Congress"); JA645 (states cannot "second-guess the FDA's explicit judgment on how to manage risks from and safely prescribe, dispense, and administer" a REMS drug).

Still elsewhere, and at odds with their other characterizations of her position, intervenors accuse Dr. Bryant of advocating a "maximalist view of the REMS" under which the REMS "set[] a federal maximum" or "ceiling" that precludes "*any* additional state restriction on a REMS drug." Resp./Reply Br. 6, 13–14 (emphasis added); *see also id.* at 2, 7, 19, 26. As Dr. Bryant has explained time and again, that is not her claim. *See, e.g.*, Bryant Br. 44–45. She simply contends that states cannot impose restrictions on a REMS drug that FDA considered and rejected and that interfere with FDA's efforts to facilitate patient access.[2]

Parties in litigation should deal with their opponents' arguments forthrightly, and intervenors' refusal to do so speaks to the weakness of their position.

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[2] In an amicus brief, forty pharmaceutical companies, executives, and investors go further and argue that the REMS is so comprehensive that it establishes "*both a floor and a ceiling*" for state requirements. Pharm. Cos. Amicus Br. 9. But even those amici acknowledge that "the Court here need not reach this conclusion to find for" Dr. Bryant, because North Carolina's restrictions are ones FDA has "*considered and rejected*." *Id.*

II. North Carolina's restrictions that are the subject of Dr. Bryant's cross-appeal are preempted.

A. Under *Geier* and *Williamson*, a state may not impose restrictions an agency has rejected as contrary to federal regulatory objectives.

As Dr. Bryant explained, this case is on all fours with *Geier*. There, the Department of Transportation considered and rejected an "'all airbag'" standard and instead "deliberately provided [car manufacturers] with a range of choices among different passive restraint devices" because it concluded that this would promote "the law's congressionally mandated objectives." 529 U.S. at 872, 875, 879. Here, in order to promote the congressionally mandated objectives of "[a]ssuring access and minimizing burden," especially for "patients who have difficulty accessing health care," 21 U.S.C. § 355-1(f), FDA considered the same restrictions on mifepristone North Carolina imposes and deliberately rejected them, instead giving prescribers and patients a range of choices about how to provide and obtain mifepristone—including via telemedicine and from federally certified pharmacies. *See* Bryant Br. 4–5, 27–28, 56–57.

Unable to distinguish *Geier*, intervenors claim for the first time (at 12) that the Supreme Court "limited *Geier* to its facts" in *Williamson*

v. Mazda Motor of America, Inc., 562 U.S. 323 (2011), a case intervenors did not cite in their initial brief to this Court or any of their briefs in the district court. *Williamson*, however, supports Dr. Bryant's claim.

Williamson reaffirmed *Geier*'s central holding that where (as here) a federal agency rejects imposing a particular requirement and instead "leaves [regulated parties] with a choice" in order "to further significant regulatory objectives," a state law imposing that requirement is invalid "[u]nder ordinary conflict pre-emption principles." *Id.* at 330, 332, 336. In *Williamson*, the Court considered a DOT regulation that declined to mandate lap-and-shoulder seatbelts for rear inner car seats. The Court held that the regulation did not preempt a state from requiring lap-and-shoulder belts, but only because "providing manufacturers with this seatbelt choice [was] not a significant objective of the federal regulation." *Id.* at 326.

The *Williamson* Court was careful to distinguish *Geier*. It explained that in *Geier*, the regulatory history showed that DOT "thought it important to leave manufacturers with a choice" between different passive restraint mechanisms. *Id.* at 330. In other words, "giving auto manufactures a choice … was a *significant objective* of the federal

regulation." *Id.* By contrast, in *Williamson*, "unlike *Geier*," it was apparent that DOT "had no interest in ensuring" manufacturer choice. *Id.* at 332–33. Although the agency had declined to mandate lap-and-shoulder belts, it had no objection to such a requirement: It "was not concerned about consumer acceptance; it was convinced that lap-and-shoulder belts would increase safety; it did not fear additional safety risks from use of those belts; it had no interest in ensuring a mix of devices; and, though it was concerned about additional costs, that concern was diminishing." *Id.* at 333.[3]

In short, *Williamson* stands for the same principle as *Geier*: When a federal agency exercising authority granted to it by Congress considers and rejects a particular requirement in order to achieve a "significant federal regulatory objective," a state is preempted from imposing that same requirement. *Id.* at 330; *see also POM Wonderful LLC v. Coca-Cola*

[3] Intervenors quote Justice Sotomayor's solo concurring opinion in *Williamson* (at 11, 34). That opinion is not controlling, but in any event, Justice Sotomayor's reasoning is similar to the majority's. She explained that under *Geier*, courts should "find pre-emption where evidence exists that an agency has a regulatory objective … whose achievement depends on [regulated parties] having a choice between options." 562 U.S. at 338. Because in *Williamson*, unlike in *Geier*, the state requirement did "not present an obstacle to any 'significant federal regulatory objective,'" Justice Sotomayor concluded it was not preempted. *Id.* at 338–39.

Co., 573 U.S. 102, 120 (2014) (under *Geier*, state law is preempted if "the FDA has … made a policy judgment that is inconsistent with" the state's requirement).

B. FDA rejected the restrictions at issue to assure patient access, which is a significant objective of both the REMS statute and the Mifepristone REMS.

The standard for preemption under *Geier* and *Williamson* is easily met here. FDA considered the same restrictions North Carolina seeks to impose, and it rejected them in order to achieve a significant regulatory objective: providing access to mifepristone without undue burdens on patients, especially rural and medically underserved patients and others who have difficulty accessing healthcare. Ensuring patient access to REMS drugs is a significant objective of both the REMS statute and the Mifepristone REMS. The text of the statute makes clear that avoiding unnecessary burdens on patient access to safe and effective drugs is a significant federal objective. *See* 21 U.S.C. § 355-1(f); Bryant Br. 8–13, 32–34. And, like in *Geier* and unlike in *Williamson*, the record here leaves no doubt that FDA "thought it important" to free patients and providers from the restrictions at issue and give them "a choice" between meeting with a REMS-certified prescriber in person or via telemedicine and

obtaining the drug from the prescriber or from a REMS-certified pharmacy. *Williamson*, 562 U.S. at 330; *see* Bryant Br. 13–17, 35–43, 60–65.

1. *The REMS Statute.* The REMS statute's many textual references to ensuring patient access make clear that this was an important objective of Congress when it crafted the statute. Intervenors try to dismiss this powerful textual evidence by insisting (at 8) that the statute's access-related provisions "limit[] only the FDA" and do not expressly mention the states. But as Dr. Bryant pointed out, that was also true in *Geier*; and if the statute expressly limited the states, this would be an *express* preemption case instead of an *implied* preemption case. An "express statement of pre-emptive intent" is not necessary for implied preemption. *Geier*, 529 U.S. at 884; *see* Bryant Br. 50–51.[4]

[4] Intervenors quote a statement in *GenBioPro, Inc. v. Sorsaia*, 2023 WL 5490179, at *6 (S.D. W. Va. Aug. 24, 2023), that the REMS statute's access-related provisions are "limitation[s] on the FDA's *own restrictions* on a drug." Resp./Reply Br. 8. But they fail to note that in the very same opinion, the court concluded that a state "restriction on prescribing mifepristone via telemedicine" is "unambiguously preempted" because the REMS "reflects a determination by the FDA that when mifepristone is prescribed, it may be prescribed via telemedicine." 2023 WL 5490179, at *10.

Attempting to refute this principle, intervenors claim (at 3) that *Virginia Uranium, Inc. v. Warren*, 587 U.S. 761 (2019), holds that even for implied obstacle preemption, Dr. Bryant must "show textual evidence that Congress intended to displace state law." But they misunderstand *Virginia Uranium*. There, the plaintiff claimed that the federal Atomic Energy Act, which regulates the use and disposal of uranium, preempted a state law that banned uranium mining. *Id.* at 765. The Court rejected that argument in a pair of three-Justice plurality opinions, both of which reject preemption for the same basic reason: the federal and state laws at issue regulated *different activities*. *See id.* at 777–79 (Gorsuch, J.) (federal law regulates uranium "*after* [it] is removed from the earth" but "doesn't touch on mining"); *id.* at 791 (Ginsburg, J.) (the federal government "does not regulate … uranium mining," so "federal law struck *no* balance in this area").[5]

[5] While Justice Gorsuch's opinion for himself and Justices Thomas and Kavanaugh announced the Court's judgment, that opinion is entitled to no more weight than the separate opinion of Justices Ginsburg, Kagan, and Sotomayor. And to the extent the opinions differ, Justice Ginsburg's is controlling because it rests on the "narrowest grounds." *White Coat Waste Project v. Greater Richmond Transit Co.*, 35 F.4th 179, 198 n.15 (4th Cir. 2022) (quoting *Marks v. United States*, 430 U.S. 188, 193 (1977)).

This case is nothing like *Virginia Uranium*. North Carolina is not regulating "an activity … far removed from" federal regulation. *Id.* at 773 (Gorsuch, J.). Instead, it is regulating the same activities FDA regulates under the REMS—the prescribing, dispensing, and administering of mifepristone—and doing so in ways FDA has considered and rejected. This would be like if instead of banning uranium *mining*, Virginia had restricted uranium *milling*—a federally regulated activity—by requiring safety measures that the responsible federal agency had determined were unnecessary and counterproductive. *See id.* at 790 (Ginsburg, J.) ("The mining ban sets no safety standards for federally supervised milling or tailings storage activities."). Nothing in *Virginia Uranium* suggests that the statute would have to *expressly* mention state law in order for such a law to be *impliedly* preempted.

Intervenors' other arguments about the statute are equally unpersuasive. Mystifyingly, they continue to invoke (at 8–10) the saving clause in the Drug Amendments of 1962 but do not even try to refute any of the points Dr. Bryant made about it. To review: (1) The plain text of the clause limits only the preemptive effect *of the 1962 amendments* and does not apply to the REMS statute enacted 45 years later; (2) Congress

deliberately adopted that textual limitation on the clause after rejecting a broader alternative proposal; (3) Congress considered including a saving clause in the REMS statute in 2007 but decided not to after FDA and others objected that it would be "counterproductive to public health for States to impose different REMS requirements than those imposed by the FDA"; and (4) even if the 1962 saving clause somehow applied to the 2007 REMS statute, the Supreme Court has held that a saving clause does not displace ordinary principles of obstacle preemption. *See* Bryant Br. 46–50 (quotation marks omitted). Intervenors' only response is to claim (at 9) that *Wyeth* disregarded the 1962 clause's express textual limitations and applied it to "the FDCA writ large," but that is false. *Wyeth* concerned the preemptive effect of the labeling provisions *in the 1962 amendments*. *See* 555 U.S. at 567. The Court thus applied the saving clause according to its text, and nothing in *Wyeth* suggests the clause governs preemption under the much-later-enacted REMS statute.

Equally strange is intervenors' claim (at 10) that Dr. Bryant "has no response" to a provision of the Food and Drug Administration Amendments Act of 2007 ("FDAAA") that expressly preempts state registration requirements for clinical trials. As Dr. Bryant explained,

that provision has nothing to do with the REMS statute: It appears in a different title of FDAAA, a broad act with many disparate components, and is codified within the Public Health Service Act, not the FDCA. *See* Pub. L. No. 110-85, § 801(d), 121 Stat. 823, 922 (2007) (codified at 42 U.S.C. § 282 note); Bryant Br. 48–49. Moreover, even if the REMS statute itself contained an express preemption provision, such a provision would "*not* bar the ordinary working of conflict preemption principles." Bryant Br. 46 (quoting *Arizona v. United States*, 567 U.S. 387, 406 (2012)). Pointing to an unrelated express preemption provision to argue against implied obstacle preemption is just another way of arguing that *all* preemption must be express, which is not the law. *See Arizona*, 567 U.S. at 406 (implied obstacle preemption is "well-settled").

Intervenors also argue (at 18–19) that Congress prohibited FDA from regulating "the practice of medicine." But the statute they rely on says only that the FDCA shall not be construed to interfere with a healthcare practitioner's "authority … to prescribe or administer any legally marketed device," which is not at issue here. 21 U.S.C. § 396. In any event, whatever limits may exist on FDA's authority to regulate medical practice, no one disputes that Congress authorized FDA to do

what it did here—reject certain restrictions on the provision of mifepristone pursuant to its duty under the REMS statute to assure patient access and minimize burdens on the healthcare system.

2. *The Mifepristone REMS.* Turning from the statute to the REMS, intervenors say (at 8) that the Mifepristone REMS contains "nary a word about mifepristone access." But FDA has recognized for decades that it is "important that women have access to medical abortion" via mifepristone, as this option "may offer women avoidance of a surgical procedure." JA115. Indeed, that is why FDA originally adopted distribution restrictions for mifepristone (which became the Mifepristone REMS)—to ensure that mifepristone could meet the criteria for approval, which was important because it provided a "meaningful therapeutic benefit to patients." JA117. And the record contains hundreds of pages of analysis by FDA concluding, based on decades of evidence, that the restrictions North Carolina seeks to impose are unnecessary and inappropriate burdens on patients' ability to access that therapeutic benefit and that patients and providers should therefore be free from these restrictions. *See* Bryant Br. 13–17, 35–43, 60–65.

For example, FDA concluded that safely prescribing mifepristone does not require an in-person examination. *See* Bryant Br. 61–62. Intervenors' response only confirms that they disagree with FDA's expert judgment. Disavowing the district court's rationale that North Carolina's in-person examination requirement is "unrelated" to "managing the safety risks of mifepristone," JA633, JA637, intervenors insist (at 31–32) that this requirement "promotes patient safety" by "allow[ing] a physician to accurately assess gestational age and diagnose an ectopic pregnancy." But FDA expressly determined that providers can "assess women for duration of pregnancy and for ectopic pregnancy" without "be[ing] physically present with the patient," including "by obtaining a medical history" and "consult[ing] with the patient over the Internet." JA240–241.

FDA also concluded that obtaining informed consent to the use of mifepristone does not require an in-person meeting. *See* Bryant Br. 62–64. Intervenors say (at 2, 34) that preemption of North Carolina's in-person informed-consent requirement depends on "tortured logic" and "vague 'notions' of agency intent," but there is nothing vague about it: FDA expressly determined that "[a] certified prescriber can … review the

Patient Agreement Form with the patient, fully explain the risks of the mifepristone treatment regimen, and answer any questions, as in any consent process, without physical proximity." *See* Bryant Br. 62–64 (quoting JA241). Intervenors simply disagree with FDA.

In rejecting these and other in-person requirements for the provision of mifepristone, FDA concluded that patients and providers should have the freedom to choose whether to meet in person or via telehealth—a freedom that is particularly important to the rural and medically underserved patients who were a particular object of congressional concern. *See* 21 U.S.C. § 355-1(f)(2)(C)(ii); HHS, *Telehealth for rural areas*, https://telehealth.hhs.gov/providers/best-practice-guides/telehealth-for-rural-areas (explaining that "[t]elehealth can help reduce health disparities by increasing access to timely, high quality health care" for the one in five Americans who live in rural or frontier areas).

Confirming the importance of that freedom to FDA's regulatory objectives, FDA did not just decline to adopt in-person requirements or remove them from the REMS after having initially imposed them. Instead, FDA went further and took positive action to facilitate patient

access via telemedicine—for example, by creating a regulatory regime whereby pharmacies can become federally certified to dispense mifepristone. *See, e.g.*, JA264 (FDA concluding that "to reduce the burden" on "healthcare providers and patients," the REMS "must be modified to remove the in-person dispensing requirement" and "allow … dispensing of mifepristone by mail via certified prescribers or pharmacies"). Intervenors do not dispute that North Carolina's restrictions would thus interfere with "the performance of activity sanctioned by federal license." *See* Bryant Br. 37–40 (quoting *Sperry v. Florida ex rel. Fla. Bar*, 373 U.S. 379, 385 (1963)).

Intervenors claim (at 1) that the fact that "FDA once found a … requirement necessary for the safe use of a drug is a point in favor of a state imposing the protection," even if FDA later rejected that requirement. That is illogical and would trap the agency's thinking in amber regardless of experience and new scientific evidence. Congress knew that some requirements initially imposed by FDA might prove unnecessary; that is why it directed FDA to "periodically evaluate" the REMS and modify them as needed to eliminate requirements that are "unduly burdensome on patient access." 21 U.S.C. § 355-1(f)(5); *see also*

id. § 355-1(g)(4). If FDA once imposed a requirement as part of the REMS, but then went to the trouble of modifying the REMS to remove that requirement, that is powerful evidence that the requirement is inconsistent with a significant federal objective.

In sum, because Congress charged FDA with assuring patient access to REMS drugs and FDA "made clear" that providing patients and providers with the choices and flexibility North Carolina seeks to deny them was "an important means for achieving [that] basic objective[]," North Carolina's restrictions are preempted. *Williamson*, 562 U.S. at 331; *accord Geier*, 529 U.S. at 881 (state airbag requirement was preempted because it was an obstacle to DOT's "important means-related federal objectives"); *Fid. Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 155 (1982) (where federal agency declined to prohibit due-on-sale clauses in mortgage contracts because it "desire[d] to afford [lenders] the flexibility to accommodate special situations and circumstances," state law restricting such clauses was obstacle-preempted because it "deprived the lender of the 'flexibility' given it by the Board" (quotation marks omitted)).

C. *Wyeth* supports Dr. Bryant's preemption claim.

Repeating word-for-word a mantra from their opening brief, intervenors say *Wyeth* "rejected the claim Plaintiff makes here: that 'the FDCA establishes both a floor and a ceiling for drug regulation.'" Resp./Reply Br. 14 (quoting *Wyeth*, 555 U.S. at 573–74). To repeat, Dr. Bryant's claim is not that the REMS operates as a "ceiling" for state regulation, but rather that states may not impose restrictions on a REMS drug that FDA has considered and rejected as unduly burdensome and that interfere with FDA's efforts to facilitate patient access to the drug. As Dr. Bryant explained, *Wyeth* supports that claim because the Court went out of its way to emphasize that "FDA did not consider and reject" the state-law requirement at issue there and to leave open the possibility that state law could have been preempted if FDA had done so. 555 U.S. at 580–81 & n.14; *see* Bryant Br. 28–30; JA651 ("[I]n *Wyeth*, the FDA had not considered and rejected the exact requirements the state [sought] to impose, a factor the Supreme Court deemed important enough to mention explicitly.").

Intervenors try to dismiss this by asserting (at 14) that Dr. Bryant "confuses obstacle preemption with impossibility preemption." But *Wyeth*

involved claims of both obstacle and impossibility preemption, and the Supreme Court made the statements in question in the course of discussing *obstacle* preemption. Responding to Wyeth's contention "that this case resembles *Geier* because the FDA determined that no additional warning on IV-push administration was needed," the Court held that Wyeth's obstacle-preemption argument failed in that case because "FDA did not consider and reject a stronger warning against IV-push injection of Phenergan." 555 U.S. at 581 n.14.

The Court thus recognized that even in the context of a non-REMS drug, principles of obstacle preemption might well bar a state from imposing a restriction that FDA *had* considered and rejected. The argument for obstacle preemption is even stronger in the context of a REMS drug like mifepristone, which is subject to federal oversight and access-focused congressional mandates that do not apply to non-REMS drugs. *See* Bryant Br. 45–46. Intervenors do not dispute that FDA has carefully considered and rejected the restrictions North Carolina seeks to impose, so this is not a case where "the record shows that the FDA has paid very little attention to the[se] issues." *Wyeth*, 555 U.S. at 581 n.14. *Wyeth* therefore supports Dr. Bryant's position on obstacle preemption.

Moreover, intervenors do not dispute that under *Wyeth*'s separate analysis of *impossibility* preemption, North Carolina would be preempted from requiring mifepristone's label to incorporate the state's restrictions. *See* Bryant Br. 30–31. For example, if a North Carolina law required that mifepristone's label limit the approved indication to patients who had undergone an in-person examination and an ultrasound, everyone agrees the law would be preempted. But according to intervenors, the state has an easy workaround—it can impose the same preempted requirements directly on federally certified mifepristone prescribers. If intervenors' position were adopted, any state could impede access to federally approved drugs by imposing restrictions that FDA has considered and rejected, so long as it did not require those restrictions to be included in the drug's label. Allowing that end-run around preemption makes no sense. And as the industry amici explain, the resulting "patchwork of restrictions on pharmaceutical products" would not only harm patients and providers but also destroy the "stability and certainty" that is "critical to maintaining pharmaceutical industry investment in innovation." Pharm. Cos. Amicus Br. 1, 16.

Nothing in *Wyeth* or any other decision requires that counterintuitive result. As explained above, *Wyeth*'s holding of no obstacle preemption was expressly limited to circumstances where FDA did *not* consider and reject the requirement at issue. The Supreme Court was careful to leave open that state-law requirements FDA *did* consider and reject might be obstacle-preempted, even for non-REMS drugs. No court has held otherwise, and this Court should not be the first.

D. It is intervenors' position, not Dr. Bryant's, that would radically alter the federal-state balance.

Intervenors' sweeping denial of preemption would represent a transformative change in the law. *Geier*, *Williamson*, and *Wyeth* all strongly indicate that states are not free to restrict the provision or distribution of federally approved drugs in ways that FDA has considered and rejected. No court has ever held that a state can impose such restrictions, even on a more lightly regulated non-REMS drug. And states hardly ever impose such restrictions, no doubt correctly recognizing that they would interfere with the carefully calibrated federal scheme and be preempted. Yet intervenors' position would mean states could impose such restrictions at will on any drug for essentially any reason. Intervenors even go so far as to proclaim (at 16) that the resulting

"patchwork" of state laws disagreeing with FDA's expert judgments would be a "feature" of their position, "not a bug." On the contrary, a 50-state patchwork would be disastrous for patient access to important medicines.

On the other side of the ledger, accepting Dr. Bryant's narrow claim in this case would mean only that for the small percentage of drugs with REMS, states could not impose restrictions that FDA has considered and rejected and that interfere with FDA's efforts to assure patient access to the drug. This Court can and should reserve any broader preemption questions for another day.

To argue otherwise, intervenors continue to misrepresent the scope and implications of Dr. Bryant's claim. They assert (at 19–20) that her theory would "run riot through state health and safety codes" because it would preempt "almost any additional state regulation on a REMS drug." That is simply untrue; as Dr. Bryant has explained, her claim is focused on requirements that FDA has considered and rejected and that would interfere with FDA's attempts to assure patient access. *See* Part I, *supra*. Underscoring the narrowness of Dr. Bryant's claim, intervenors have

abandoned their reliance on the major questions doctrine, which their response/reply brief does not mention once.

Intervenors' contention (at 16–17, 24) that Dr. Bryant's claim would bar states from providing a tort remedy for consumers harmed by unsafe or ineffective drugs is likewise false. Under Dr. Bryant's theory, a tort suit could be preempted if it sought to impose a specific restriction on a REMS drug that FDA had considered and rejected as an inappropriate barrier to patient access. *See Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 492 (2013) (preemption requires "determining precisely what, if any, specific requirement a state common-law claim imposes" (quotation marks omitted)). General tort remedies for consumers injured by mifepristone would not be affected. This is clear from *Geier*: The Court's holding that a tort action was preempted if it "depend[ed] upon [a] claim that manufacturers had a duty to install an airbag," 529 U.S. at 881, did not affect the availability of a general tort remedy for consumers injured by defective cars.

Intervenors also play fast and loose with the number of state laws that could potentially be affected by Dr. Bryant's theory. For example, they claim (at 20 & n.3) that thirty-four states have enacted "informed

consent laws" regarding mifepristone. But more than half the laws they cite do not require that informed consent be obtained in person and thus do not conflict with FDA's deliberate determination that informed consent for this drug can be obtained through telehealth.[6]

Further confirming that Dr. Bryant's claim does not threaten legitimate state health-and-safety laws, seventeen states and the District of Columbia filed an amicus brief supporting that claim. These states are protective of their historic police powers and are not likely to embrace a preemption theory that would "run riot" through their laws. They recognize, however, that accepting Dr. Bryant's claim would "not mean that REMS requirements will *always* set the ceiling for regulation of a given drug." D.C. Amicus Br. 21. Rather, preemption would apply where the "specific FDA regulatory history at issue" shows that "FDA determined that … particular restrictions to access would create an

[6] *See* Alaska Stat. Ann. § 18.16.060; Conn. Agencies Regs. § 19a-116-1; Ga. Code Ann. § 31-9A-3; Idaho Code Ann. § 18-609; Iowa Code Ann. § 146A.1; Kan. Stat. Ann. § 65-6709; Ky. Rev. Stat. Ann. § 311.725; Me. Stat. tit. 22, § 1599-A(2); Mass. Gen. Laws ch. 112, § 12R; Mo. Ann. Stat. § 188.039(4); Mont. Code Ann. § 50-20-106; Neb. Rev. Stat. Ann. § 28-327; Nev. Rev. Stat. Ann. § 442.253; N.D. Cent. Code Ann. § 14-02.1-02(9); Okla. Stat. tit. 63, § 1-738.2; 18 Pa. Cons. Stat. § 3205; R.I. Gen. Laws § 23-4.7-2; S.C. Code Ann. § 44-41-30; Va. Code Ann. § 18.2-76.

obstacle to Congress's goal of expanding access to critical drugs within bounds necessary to preserve public safety." *Id.* at 22.

Grasping for some troubling consequence they can ascribe to Dr. Bryant's claim, intervenors assert (at 21–23) that state opioid laws would be preempted under her theory. But they fail to identify a single state law that imposes restrictions on opioids that FDA has considered and rejected. *First*, they say (at 23) twenty-nine states "limit the number of days' supply of opioids that can be prescribed for acute pain." But intervenors point to no evidence that FDA has rejected a maximum duration of opioid use for *acute* pain; the 2013 letter they cite discussing durational use limits was focused on opioids that were indicated exclusively to treat long-term *chronic* pain.[7] And even as to chronic pain, that letter did not consider limiting the length of each individual prescription and requiring the physician to issue new prescriptions as needed, which is all the state laws cited by intervenors do. *Next*, intervenors say (at 22) six states "limit the dosage of opioids that a

[7] *See* Letter from Janet Woodcock, MD, Dir., Ctr. for Drug Evaluation & Rsch., FDA, to Andrew Kolodny, President, Physicians for Responsible Opioid Prescribing 3, 14–17 (Sept. 10, 2013), *available at* https://perma.cc/RK2J-HTAH.

healthcare provider can prescribe." But the laws they cite allow the nominal dose limit to be exceeded if certain conditions are met, such as the pain being chronic or a physician documenting the need for a higher dose. While FDA declined to establish a rigid absolute maximum daily dose for opioids, intervenors have not pointed to any evidence that it has opined on these more nuanced and flexible dosing regulations.[8] *Finally*, intervenors say (at 22–23) eleven states "have limitations on prescribing opioids to minors," but they do not claim that FDA has rejected such limitations.[9]

In the end, intervenors cannot establish that Dr. Bryant's narrow claim would lead to the invalidation of any significant number of state

[8] *See* Letter from Janet Woodcock at 1, 5, 11–12.

[9] Moreover, even if intervenors could identify some state opioid restriction that *FDA* has declined to impose (which they have not done), that would not be the end of the analysis. Unlike mifepristone, the provision and distribution of which is regulated at the federal level exclusively through the federal REMS, opioids are controlled substances governed by a complex web of federal statutes and regulations implemented by numerous agencies, including the DEA and the CDC. *See, e.g.*, Letter from Janet Woodcock at 2 & nn.8–9; CDC, *New 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain* (Nov. 17, 2022), https://www.cdc.gov/coca/hcp/trainings/guideline-prescribing-opioids-pain.html. So the preemption analysis for opioids would be far more complex.

laws. And to the extent a few states have taken the unusual step of imposing restrictions on mifepristone (or another REMS drug) that FDA has considered and rejected because those restrictions create unwarranted barriers to patient access, it should come as no surprise that such laws are on shaky ground under *Geier*, *Williamson*, and *Wyeth*.

III. Dr. Bryant has a cause of action for her cross-appeal.

Intervenors' argument that Dr. Bryant lacks a cause of action is forfeited and meritless. Intervenors argue for the first time (at 39) that their forfeiture should be excused because they are raising a non-forfeitable "fundamental error." This argument comes too late, and regardless, it is well-established that a defendant's contention that a plaintiff lacks a cause of action can be forfeited. *See, e.g.*, *Air Courier Conf. v. Am. Postal Workers Union, AFL-CIO*, 498 U.S. 517, 522–23 & n.3 (1991) (refusing to consider unpreserved no-cause-of-action argument); *Hicks v. Ferreyra*, 965 F.3d 302, 310–12 (4th Cir. 2020) (same).

On the merits, intervenors make a hash of the law. They claim that Dr. Bryant has no cause of action because "'the Supremacy Clause is not the source of any federal rights'" and "a federal cause of action cannot exist absent a federal right." Resp./Reply Br. 37 (quoting *Armstrong v.*

Exception Child Ctr., Inc., 575 U.S. 320, 324 (2015)). This syllogism is wrong. As intervenors' own cited case explains, although "the Supremacy Clause is not the 'source of any federal rights,'" this does not "diminish the significant role that courts play in assuring the supremacy of federal law" because "as we have long recognized," an equitable cause of action is still available to enjoin the enforcement of preempted state law. *Armstrong*, 575 U.S. at 324–27 (citing *Ex parte Young*, 209 U.S. 123, 155–56 (1908)).

Dr. Bryant thus has an equitable cause of action to enjoin the enforcement of North Carolina's preempted laws. And the FDCA does not limit that cause of action because, as Dr. Bryant explained and intervenors do not dispute, her suit is not a proceeding "for the enforcement, or to restrain violations, of" the FDCA within the meaning of 21 U.S.C. § 337(a). *See* Bryant Br. 73–76.

IV. North Carolina should be enjoined from enforcing any provision of state law that imposes the restrictions challenged in Dr. Bryant's cross-appeal.

If this Court concludes that the restrictions challenged in Dr. Bryant's cross-appeal are preempted, it should direct the district court to permanently enjoin North Carolina from enforcing any provisions of

state law that impose those restrictions, regardless of where in the North Carolina codebooks they may be found. *See* Bryant Br. 76–79.

Intervenors cite no case from this Court or any other court holding that such an injunction is improper. In *Hayes v. North State Law Enforcement Officers Ass'n*, 10 F.3d 207, 217 (4th Cir. 1993), the injunction was overbroad because it enjoined conduct—the use of racial employment criteria other than the challenged policy—that had not been determined to be unconstitutional. In *Schmidt v. Lessard*, 414 U.S. 473, 476 (1974) (per curiam), the injunction was simply "too vague to be understood." And in *Bostic v. Schaefer*, 760 F.3d 352, 369 (4th Cir. 2014), the Court affirmed the district court's injunction without addressing whether a broader injunction would have been permissible.

Here, an injunction prohibiting enforcement of the challenged restrictions would be easily understood and would not prohibit any potentially constitutional conduct. Intervenors concede that any provision of North Carolina law, whether currently on the books or enacted in the future, that imposes "'the same preempted restrictions'" challenged here "would be governed by" the decision in this case.

Resp./Reply Br. 41 (quoting Bryant Br. 78). So there is no logical reason why an injunction in this case should not apply to such provisions.

CONCLUSION

This Court should affirm with respect to the restrictions the district court held were preempted, reverse with respect to the restrictions the court held were not preempted, and remand for the court to permanently enjoin enforcement of the latter.

Respectfully submitted,

/s/Eva A. Temkin

Paul Alessio Mezzina
KING & SPALDING LLP
1700 Pennsylvania Avenue NW
Washington, DC 20006
(202) 737-0500
pmezzina@kslaw.com

Eva A. Temkin
ARNOLD & PORTER KAYE SCHOLER LLP
601 Massachusetts Avenue NW
Washington, DC 20001
(202) 942-5123
Eva.Temkin@arnoldporter.com

Nicole L. Masiello
ARNOLD & PORTER KAYE SCHOLER LLP
250 West 55th Street
New York, NY 10019
(212) 836-7876
nicole.masiello@arnoldporter.com

Counsel for Amy Bryant, M.D.

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Fed. R. App. P. 28.1(e)(2)(C) because it contains 6,420 words, excluding the parts of the brief exempt by Federal Rule of Appellate Procedure 32(f).

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/s/Eva A. Temkin
Eva A. Temkin

Counsel for Amy Bryant, M.D.