No. 23-2194

IN THE UNITED STATES COURT OF APPEALS FOR THE FOURTH CIRCUIT

GENBIOPRO, INC.,
Plaintiff-Appellant,

v.

KRISTINA D. RAYNES, *in her official capacity as Prosecuting Attorney of Putnam County*, AND PATRICK MORRISEY, *in his official capacity as Attorney General of West Virginia*,
Defendants-Appellees.

On Appeal from the United States District Court
for the Southern District of West Virginia (Huntington),
No. 3:23-cv-00058, Hon. Robert C. Chambers

REPLY BRIEF OF PLAINTIFF-APPELLANT GENBIOPRO, INC.

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INTRODUCTION

In 2007, Congress decided that a small category of drugs could be made accessible to patients safely, so long as FDA authoritatively determined the standards for access. This case concerns that federal regime, codified in the FDAAA. *See* 21 U.S.C. 355-1 *et seq*.

The statute authorizes FDA to control these drugs' prescription and dispensing by imposing safe-use elements. It leaves no room for states to regulate drugs approved with such elements. Under the FDAAA, FDA must weigh the burdens any necessary safety restrictions impose on patients' access to these drugs, and it must minimize burdens on the healthcare system. Congress requires the agency to update and reevaluate its restrictions regularly. But FDA cannot fulfill this mandate if it must act against an ever-changing array of state restrictions on such drugs.

West Virginia imposes a near-total ban on patients' access to one of the drugs FDA regulates with safe-use elements: mifepristone. FDA approved mifepristone only for abortion, but West Virginia prohibits virtually all abortions and imposes criminal penalties on healthcare professionals who provide the drug for that purpose.

The challenged laws are preempted. They intrude on a field Congress reserved for FDA and make it impossible for GenBioPro to provide mifepristone in accordance with FDA's specifications. And they undermine Congress's goal of imposing only those burdens on access to mifepristone that FDA determines are necessary for its safe use.

Appellees do not engage with Congress's detailed commands in the FDAAA. Instead, they frame this case as a challenge to states' historic power to protect their citizens' health. But the state statutes in question are not general health regulations. In prohibiting nearly all abortions, they functionally ban mifepristone for its sole FDA-approved use. The laws interfere with FDA's regulation of mifepristone and with Congress's mandate that FDA alone weigh the burdens any restrictions impose on patients and healthcare providers.

Appellees alternately protest that West Virginia's laws do not regulate mifepristone and that, because mifepristone is indicated for abortion, it should be treated differently from other drugs. But West Virginia expressly restricts medications used for abortion, and FDA approved only one drug for that purpose. Neither the Supremacy Clause nor the FDAAA contains an exception for abortion.

Drugs with safe-use elements are a creature of federal law, regulated at the federal level. In arguing otherwise, Appellees egregiously mischaracterize history and the FDAAA. States never approved drugs or banned drugs for their federally approved uses, much less drugs with safe-use elements.

The district court properly upheld GenBioPro's standing. West Virginia's unconstitutional restrictions prevent GenBioPro from selling mifepristone in the State and restrict providers' ability to prescribe and dispense it. GenBioPro has a cause of action in equity to remedy that injury, and Appellees have forfeited any argument otherwise.

ARGUMENT

I. CONGRESS PREEMPTED WEST VIRGINIA'S RESTRICTIONS ON MIFEPRISTONE

The FDAAA preempts West Virginia's restrictions on mifepristone. *First*, it occupies the narrow field of regulating drugs with safe-use elements, a category that includes mifepristone. Congress gave FDA granular instructions regarding how to balance access and burden considerations and listed the factors the agency must consider in doing so. By delegating authority to FDA to determine appropriate

restrictions on these medications, Congress signaled a dominant federal interest and a desire for national uniformity in their regulation.

A patchwork of varying state restrictions like West Virginia's prevents FDA from engaging in the balancing Congress demands and renders the FDAAA's goal of creating national uniformity all but meaningless. The statute's text recognizes Congress's intent that drugs with safe-use elements be accessible to patients, subject to FDA's judgment reconciling safety needs with burdens on patients' access and the national healthcare delivery system.

Second, West Virginia's restrictions on mifepristone conflict with those FDA implemented. They make it impossible for GenBioPro to sell its product in the State and penalize GenBioPro's customers for providing mifepristone in accordance with its REMS.

The restrictions also undermine Congress's goals in the FDAAA. Congress codified, and authorized FDA to implement, national criteria in determining when patients can access drugs with safe-use elements. FDA made the required determinations for mifepristone, reflected in

the 2023 Mifepristone REMS.[1] West Virginia's restrictions conflict with the REMS by limiting access to mifepristone, when FDA has concluded it should be accessible and has eased restrictions on the drug.

A. Congress Occupied The Limited Field Of Regulating Drugs With Safe-Use Elements

Congress's "intent to displace state law altogether can be inferred" either (1) from a framework of regulation so pervasive that Congress left no room for the States to supplement it or" (2) when the regulatory field concerns a dominant federal interest. *Arizona v. United States*, 567 U.S. 387, 399 (2012); *accord Ray v. Atlantic Richfield Co.*, 435 U.S. 151, 161, 163 (1978). The preempted field can be vast (e.g., immigration) or narrow (e.g., safety standards for workers handling hazardous waste). *Compare Arizona*, 567 U.S. at 400, *with Gade v. National Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 108 (1992).[2]

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[1] *REMS Single Shared System for Mifepristone 200 mg* at 1, FDA (Mar. 2023) ("2023 Mifepristone REMS"), https://www.accessdata.fda.gov/drugsatfda_docs/rems/Mifepristone_2023_03_23_REMS_Full.pdf.

[2] Congress may define "the scope of a field deemed preempted by federal law . . . narrowly." *Farina v. Nokia Inc.*, 625 F.3d 97, 121 n.25 (3d Cir. 2010); *see also* Opening Br. 53-55 (citing examples). Appellees ignore the key Supreme Court case finding preemption of narrow fields, *United States v. Locke*, 529 U.S. 89 (2000).

As relevant here, within the broad arena of "regulati[ng] . . . health and safety," "the Federal Government can set uniform national standards" in specific areas that preempt state law. *Gonzales v. Oregon*, 546 U.S. 243, 270-71 (2006); *see*, *e.g.*, *Gade*, 505 U.S. at 108 (occupational health and safety).

1. The FDAAA imposes comprehensive regulation in an area with a dominant federal interest

a. In enacting a "comprehensive . . . scheme of federal regulation" for drugs that cannot be approved without safe-use elements, Congress occupied a limited field. *Ramah Navajo Sch. Bd., Inc. v. Bureau of Revenue of N.M.*, 458 U.S. 832, 836 (1982). The FDAAA vested FDA with exclusive authority to regulate these drugs and specified the relevant considerations for FDA to assess. *See generally* 21 U.S.C. § 355-1. Congress authorized FDA alone to determine the elements required to assure these drugs' safe use while minimizing specified burdens.

The FDAAA delineates which FDA personnel must decide whether a REMS with safe-use elements is necessary, the factors FDA must consider in imposing one, components it may include, and how often the agency must reevaluate it. *Id.* § 355-1(a), (c), (e), (f). After

determining safe-use elements are warranted, FDA dictates who can prescribe the drug and how, which patients can receive it, where and how it is dispensed, and how patients take it. *Id.* § 355-1(f). FDA may, for example, require patients to obtain lab results or complete questionnaires before receiving the drug,[3] limit the permissible dosage,[4] specify how and in what quantities pharmacies may dispense,[5] and instruct patients how to dispose of unused medication.[6]

Congress requires FDA to balance any safety restrictions against burdens on patient access and the healthcare delivery system. *Id.* § 355-1(f)(2). As with other schemes calibrated to protect "competing interests," the FDAAA preempts the field of regulating drugs with safe-use elements. *PPL EnergyPlus, LLC v. Nazarian*, 753 F.3d 467, 473,

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[3] *Ambrisentan Shared System REMS Program* at 3-4, FDA (June 2021), https://www.accessdata.fda.gov/drugsatfda_docs/rems/Ambrisentan_Shared_System_2021_06_08_REMS_Full.pdf; *Isotretinoin (iPLEDGE®) Shared System REMS Program* at 2-3, FDA (Oct. 2023), ("Isotretinoin REMS"), https://www.accessdata.fda.gov/drugsatfda_docs/rems/Isotretinoin_2023_10_03_REMS_Full.pdf.

[4] *Lenalidomide REMS Program* at 2-3, 8, FDA (Mar. 2023), https://www.accessdata.fda.gov/drugsatfda_docs/rems/Lenalidomide_2023_03_24_REMS_Full.pdf.

[5] *Id.* at 2-3, 7-8, 137-39.

[6] *Id.* at 4.

475-76 (4th Cir. 2014), *aff'd sub nom. Hughes v. Talen Energy Mktg., LLC*, 578 U.S. 150, 136 (2016); *see id.* at 473 (finding preemption warranted when Congress enacted "comprehensive program of regulation . . . quite sensitive to external tampering"). Such regimes leave "no room either for direct state regulation" or indirect rules that "achieve the same result." *Id.* at 475.

b. Congress signals a dominant federal interest when it vests "exclusive [regulatory] authority" in a federal agency to create "uniform national standards" governing a field. *Ray*, 435 U.S. at 159, 163. In the FDAAA, Congress conveyed a dominant federal interest in assuring that nationwide, uniform rules govern patients' access to drugs with safe-use elements.

Congress directed FDA to apply specific criteria and "balance a number of considerations" in crafting safe-use elements. *Id.* at 177; *see* 21 U.S.C. § 355-1(f)(1). These criteria implicate national concerns, applicable across state lines: FDA must consider patients "with serious or life-threatening diseases or conditions," "in rural or medically underserved areas," and "with functional limitations." 21 U.S.C. § 355-1(f)(2)(C). It must reduce burdens on the "health care delivery system."

Id. § 355-1(f)(2)(D). And it must determine whether providers and pharmacies prescribing and dispensing the drug must be specially trained or certified nationwide. *Id.* § 355-1(f)(3)(A)-(B).

To make this balancing possible, the FDAAA federalizes areas "normally left to the discretion of the medical community." Amicus Br. of Doctors for Am. at 8, Dkt. 33-1. This enables FDA to ensure safe-use elements do not unduly burden patient access or the healthcare delivery system. *See id.* at 5 (describing burdens on medical profession).

FDA made these determinations for mifepristone. The resulting REMS requires providers and pharmacies to be specially certified and agree to prescribe or dispense mifepristone in "compliance with the Mifepristone REMS."[7] *See* Opening Br. 12-14.

2. West Virginia regulates access to mifepristone

The UCPA seeks to dictate how and to whom mifepristone may be prescribed and dispensed. W. Va. Code §§ 16-2R-1 *et seq.*, 61-2-8. It substitutes West Virginia's judgment for FDA's and intrudes on a field necessitating national uniformity.

[7] 2023 Mifepristone REMS, *supra* note 1, at 8.

Appellees argue (at 29) that the UCPA regulates abortion, not mifepristone, and therefore implicates a different field. But "[p]re-emption is not a matter of semantics"; it concerns a law's "operation and effect," regardless of its title or the state's characterization in litigation. *Wos v. E.M.A. ex rel. Johnson*, 568 U.S. 627, 636 (2013); *see also National Meat Ass'n v. Harris*, 565 U.S. 452, 464 (2012) (a state cannot "escape preemption" by "framing" its law to regulate what federal law does not).

Abortion is the only approved indication for mifepristone, the only drug FDA approved to terminate pregnancy.[8] In banning almost all abortions, the UCPA functionally bans mifepristone's use and sale. Despite Appellees' suggestion (at 30) that the UCPA "does not mention mifepristone," the UCPA defines abortion as "the use of any . . . medicine, drug, or any other substance . . . with intent to terminate . . . pregnancy." W. Va. Code § 16-2R-2. Mifepristone fits that bill.

Appellees argue (at 29-30) that the UCPA is a permissible "upstream" regulation, citing *Virginia Uranium, Inc. v. Warren*, 139 S. Ct. 1894, 1914-15 (2019) (Ginsburg, J., concurring in the judgment). In

[8] 2023 Mifepristone REMS, *supra* note 1, at 1.

Virginia Uranium, Congress occupied the field of uranium milling (how uranium is refined), but not the field of uranium *mining* (how it is extracted). *Id.* at 1910; *see id.* at 1900 (plurality op. of Gorsuch, J.) (same). The state law concerned only mining, not milling, so it was not preempted. *Id.* at 1901-02 (noting federal law regulates "nearly every aspect of the nuclear fuel life cycle *except* mining").

Here, federal and state law regulate the same subject: access to mifepristone. Unlike uranium mining, this is not an area Congress "chose to leave alone." *Id.* at 1900. In the FDAAA, Congress authorized FDA to regulate every step of mifepristone's use.

3. Appellees' remaining field preemption arguments are unavailing

a. Appellees contort history in arguing (at 31-32) that regulating safe-use drugs is not an area of historical federal concern, so "traditional state laws" regulating health and medicine prevail. That erroneous contention ignores the federal government's role in deciding which drugs to approve for more than a century. Amicus Br. of Historians at 3-4, Dkt. 55; *see* Pure Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906) (repealed 1938).

States neither approve drugs nor restrict drugs' prescribing or dispensing for their FDA-approved uses, outside of controlled substances. And state tort remedies, which Appellees cite (at 32), must parallel federal misbranding standards in providing "appropriate relief for injured consumers." *Wyeth v. Levine*, 555 U.S. 555, 574 (2009).

Appellees' reference (at 34) to state opioid regulations is inapposite. Opioids are subject to the Controlled Substances Act, 21 U.S.C. §§ 801-904, which sets legal rules not at issue here. *See Gonzales*, 546 U.S. at 270. Appellees argue that states may restrict access to drugs with safe-use elements because they are "the most high-risk." But Congress disagreed and determined that FDA alone should evaluate, monitor, and regulate these drugs. *See* 21 U.S.C. § 355-1(f)(2)(C)-(D).

b. Appellees argue (at 32-33) that the savings clause in the FDCA's 1962 amendments defeats preemption. But "that savings clause applied by its terms only to the 1962 amendments." *Bryant v. Stein*, 2024 WL 1886907, at *19 (M.D.N.C. Apr. 30, 2024). Congress did not apply the 1962 savings clause to the 2007 FDAAA, which has no savings clause. Even if the 1962 savings clause applied, it would

merely preserve state tort remedies with respect to drugs approved with safe-use elements.[9]

B. The UCPA Conflicts With The FDAAA And FDA's Determinations

A state statute that "conflict[s] with a federal statute" is preempted. *Crosby v. National Foreign Trade Council*, 530 U.S. 363, 372 (2000). As Congress required, FDA regulates mifepristone with safe-use elements specifying how patients may receive the drug and how healthcare professionals may prescribe and dispense it. *See* Opening Br. 30. The UCPA strikes a different balance, functionally banning the drug.

1. The UCPA makes it impossible to provide mifepristone in accordance with the REMS

While FDA approved prescribing mifepristone through 70 days' gestation, the UCPA forbids that. JA318 (¶ 70). Healthcare

[9] Appellees' amici suggest, incorrectly, that mifepristone was approved with a "voluntary" safety protocol. Amicus Br. of Family Rsch. Council et al. at 11-12, Dkt. 67-1. GenBioPro's mifepristone has been subject to a REMS since its approval, and FDA approved branded mifepristone subject to Subpart H's mandatory safety requirements. Opening Br. 12; JA310 (¶ 39); Letter from Ctr. for Drug Evaluation & Rsch., FDA, to S. Arnold, Vice President, Population Council at 1 (Sept. 28, 2000), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2000/20687appltr.pdf.

professionals who comply with mifepristone's REMS when prescribing or dispensing the drug to patients but act outside the UCPA's limited exceptions violate state law.

a. Appellees argue (at 15, 35-36) that the UCPA does not regulate GenBioPro or apply "to the commercial distribution of mifepristone in West Virginia." But the statute regulates *any person* who performs or attempts to induce an abortion in the State. W. Va. Code § 16-2R-2. It regulates "licensed medical professional[s]," who face penalties for violating the statute by prescribing GenBioPro's medication. *Id.* §§ 16-2R-7, 61-2-8(a); *see* GenBioPro's Opp. to Sorsaia's Mot. to Dismiss at 11, (S.D. W. Va. Mar. 7, 2023), Dkt. 31. And its vague definition of "[a]ttempt to perform" an abortion includes "an act or the omission of an act that, under the circumstances as the person so acting or omitting to act believes them to be, constitutes a substantial step in a course of conduct intended to culminate in an abortion."[10] W. Va. Code § 16-2R-2. Any "person," including a corporation, that "attempts to perform or induce an abortion," as the UCPA defines it,

[10] Contrary to Appellees' assertion (at 35-36), GenBioPro made this argument before the district court. *See* JA133-134.

commits a felony. *Id.* § 61-2-8(a); *see id.* § 2-2-10(a)(9); JA318-319 (¶ 71). Each time GenBioPro provides mifepristone, it takes a step aimed at providing abortion care.[11]

Appellees have stated publicly that they intend to enforce the State's abortion laws. JA115, JA305-306 (¶¶ 24-25). They now graft onto the statute a requirement that GenBioPro know whether its product will be used in an "illegal" abortion. Opp. 36. But the law criminalizes any person other than a "licensed medical professional . . . who knowingly and willfully . . . attempts to perform or induce an abortion," whether or not the abortion is legal. W. Va. Code § 61-2-8(a); *see* Opening Br. 40-41 & n.27.

b. Appellees' claim (at 36-37) that this case concerns whether the FDAAA mandates access to mifepristone is misplaced. The FDAAA

[11] Appellees argue (at 38) that GenBioPro's drug can be prescribed for Cushing's Syndrome or uterine leiomyomas, but GenBioPro's product is not approved for either. *See* GenBioPro's Opp. to Morrisey's Mot. to Dismiss at 16 & n.10, (S.D. W. Va. Mar. 17, 2023), Dkt. 35. Korlym, approved for Cushing's Syndrome, is a different drug, not subject to a REMS. *Id.* Appellees' argument illustrates the danger posed by "the unscrupulous use of extrinsic [evidence] to resolve competing theories against the complaint." *Khoja v. Orexigen Therapeutics, Inc.*, 899 F.3d 988, 998 (9th Cir. 2018). On a motion to dismiss, all inferences should be drawn in GenBioPro's favor.

does not *mandate* unlimited access to any drug; rather, it *delegates* to FDA sole authority to determine whether and how patients access certain drugs. This is analogous to the federal Ports and Waterways Safety Act in *Locke*, in which Congress delegated to the Coast Guard authority to "promulgate[] its own requirement[s]" regulating oil tankers or "decide[] that no such requirement should be imposed at all." 529 U.S. at 110; *see Ray*, 435 U.S. at 177-78. When the Coast Guard required just two watchkeepers on tankers, Washington's "different rule[]" requiring more was preempted. *Locke*, 529 U.S. at 114.

Next, Appellees argue (at 37-39) that no conflict exists because federal law does not require GenBioPro to sell mifepristone, and State law does not forbid it. The Supreme Court rejected the argument that a manufacturer's ability to "simply leav[e] the market" insulates a state law from impossibility preemption. *Mutual Pharm. Co. v. Bartlett*, 570 U.S. 472, 489 (2013). When GenBioPro markets mifepristone, it must do so under FDA's balancing determinations in the REMS. The UCPA forbids that by outlawing mifepristone's provision for its approved use. *Supra* pp. 9-11. If GenBioPro tries to market mifepristone in West

Virginia, state law prohibits healthcare providers and pharmacies from providing it in almost all cases. W. Va. Code §§ 16-2R-3, 61-2-8(a).

Without citation, Appellees argue (at 38) that *Bartlett* does not apply if a manufacturer has "not even *started* selling" in the state. But GenBioPro sells mifepristone nationwide. JA96. On a motion to dismiss, the Court must assume the facts most favorable to GenBioPro concerning its West Virginia sales. *Supra* n.11.

Finally, Appellees' analogy (at 38) to drugs "that may be used for lethal injection" is flawed. FDA cannot approve drugs for lethal injection.[12] *Contra* Amicus Br. of Ctr for L. & Just. at 2-3, Dkt. 69.[13]

2. West Virginia's restrictions interfere with Congress's determinations

The FDAAA was a groundbreaking law that "enhance[d]" FDA's "postmarket authorit[y]" to ensure access to drugs that might be associated with adverse events. FDAAA pmbl., 121 Stat. at 823. When it "deemed" mifepristone to have a REMS, Congress delegated to FDA

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[12] *See generally Whether the Food and Drug Administration Has Jurisdiction over Articles Intended for Use in Lawful Executions*, 43 Op. O.L.C., slip. op. (2019), https://www.justice.gov/olc/opinion/file/1162686/dl.

[13] This case does not implicate conscience rights or alleged "rights" of fetuses, as Appellees' amici erroneously assert.

authority to impose safe-use elements and determine how patients may receive that drug. FDAAA § 909(b)(1), 121 Stat. at 950-51, *reprinted at* 21 U.S.C. § 331 note.

The UCPA undermines Congress's goal of ensuring a uniform scheme governing access to safe-use drugs and its requirement that restrictions minimize burdens on access and the healthcare delivery system. 21 U.S.C. § 355-1(f)(2), (f)(5)(B). FDA cannot comply with Congress's requirements against multiple, ever-changing state restrictions.

a. Appellees argue (at 40-41) that the FDAAA establishes a regulatory "floor," not a ceiling. But section 355-1 vests FDA alone with authority to determine which patients may receive mifepristone, dictating where, when, and how. *See supra* pp. 6-8. Nothing in the FDAAA empowers states to countermand FDA's determinations.

Congress's use of mandatory language in instructing an agency to act — employing specific criteria — establishes a regulatory ceiling as well as a floor. For example, in *National Association of Home Builders v. Defenders of Wildlife*, 551 U.S. 644, 650-51, 663-64 (2007), Congress instructed that the EPA "shall" authorize a state to issue certain

permits after completing nine statutory criteria, which "operate[d] as a ceiling as well as a floor" — each needed to be met. *Id.* at 663.

Here, when FDA determines a drug to require a REMS, Congress specifies what FDA "shall" do, and when and how. 21 U.S.C. § 355-1(f)(2), (f)(5). The safe-use elements, like questionnaires to determine patient comprehension or prescriber knowledge and qualifications, impose a ceiling. Congress also mandated that FDA "shall . . . minimize the burden on the health care delivery system." *Id.* Any *additional* burden exceeds the ceiling FDA must determine.

Contrary to Appellees' argument (at 41-44), the FDAAA regulates safety *and* access. It enables drugs that otherwise could not be approved to enter the market, subject to the minimum burdens on access FDA determines are "necessary" (for patient access) and "practicable" (for impacts on the nationwide healthcare delivery system). 21 U.S.C. § 355-1(f).

b. Instead of addressing the FDAAA's regime for safe-use drugs, Appellees focus on other FDCA provisions. They mistakenly rely (at 41) on Congress's decision to include in the FDCA an express preemption provision governing medical devices. Yet "the existence of a

separate preemption provision does not bar the ordinary working of conflict preemption principles." *Bryant*, 2024 WL 1886907, at *19 (quoting *Hillman v. Maretta*, 569 U.S. 483, 498 (2013)).

Appellees argue (at 47) that it "makes no sense" for Congress to preempt "complementary" regulation only for drugs deemed to require safe-use elements. But to be approved, these drugs require federal post-market regulation, which FDA must re-evaluate periodically to ensure restrictions are not unduly burdensome. *See* 21 U.S.C. § 355-1(f)(5); Opening Br. 60-61. FDA cannot make the required determinations against an evolving array of state restrictions.

Congress therefore directed FDA to make uniform determinations about safety and burden on patient access and on the healthcare delivery system on a nationwide basis. Accordingly, the district court and Appellees err in reading the FDAAA as limiting only FDA's own restrictions. States' restrictions are preempted because they interfere with the "complex decisions" Congress entrusted to FDA. *International Paper Co. v. Ouellette*, 479 U.S. 481, 494-95 (1987).

In any event, the UCPA does not "complement[]" FDA's regulations. Opp. 47. The UCPA "clash[es]" with mifepristone's REMS,

regulating the drug differently than FDA mandated. *Amgen Inc. v. Sandoz Inc.*, 877 F.3d 1315, 1329 (Fed. Cir. 2017).

C. Appellees' Remaining Preemption Arguments Fail

1. No presumption applies

The district court erred in applying a presumption against preemption. The UCPA regulates in an arena that exists by virtue of federal law: access to drugs that cannot be approved without safe-use elements. Opening Br. 70-73. Appellees ignore Supreme Court precedent holding that no presumption applies in areas with "a history of significant federal presence," implicating "considerable federal interest[s]." *Locke*, 529 U.S. at 94, 108.

Appellees point to the history of state consumer protection lawsuits, but the cases they cite (at 31-32) concern state tort liability paralleling federal misbranding standards, not bans on medication. *See supra* p.12. Lacking precedent for state bans on safe-use drugs, Appellees point to states' history of regulating "health and safety." Opp. 31. But courts do not assess whether a dispute concerns "health care in general"; they ask whether it concerns matters "that arise from a federal law." *Bell v. Blue Cross & Blue Shield of Okla.*, 823 F.3d 1198, 1201-02 (8th Cir. 2016).

Appellees' assertion (at 27) that they may ban mifepristone because states criminalized abortion before *Roe v. Wade*, 410 U.S. 113 (1973), is ahistorical. Pre-*Roe* state statutes "narrowly targeted fraud and adulteration" related to poisons and unapproved "patent medicines." *See* Amicus Br. of Historians at 3-5.

Appellees cite (at 31) *Rice v. Santa Fe Elevator Co.*, 331 U.S. 218 (1947), but that case supports GenBioPro. States historically set rates and regulated grain warehouses before federal law imposed a uniform regime precluding them from "supplement[ing]" federal regulations. *Id.* at 230-31, 236. And *Altria Group, Inc. v. Good*, 555 U.S. 70 (2008), is inapposite. It concerned whether states could continue to regulate fraudulent statements even though the federal Labeling Act preempted certain failure-to-warn claims related to advertising. Opp. 26. *Altria* provides no support for the notion that states may ban safe-use drugs, as opposed to providing remedial causes of action.

2. The major questions doctrine is not implicated because Congress delegated mifepristone's regulation to FDA

The district court correctly held the major questions doctrine inapplicable because FDA "act[ed] narrowly pursuant to an explicit

grant of authority as to a single prescription medication — the FDAAA's express command that the FDA promulgate a REMS for Subpart H-approved drugs (including mifepristone), subject to certain delineated principles, including ensuring accessibility." JA262. Moreover, the court held that *Congress* "knew" mifepristone "was used only for medication abortion" and ordered FDA to regulate that drug. JA263.

Appellees argue (at 28) that GenBioPro's "theory of interpretation" "lack[s] … historical precedent." But construing the FDAAA is a matter of statutory construction; interpreting the UCPA to *negate* congressional action is unprecedented.

The cases on which Appellees rely (at 28) are inapposite. In *Alabama Association of Realtors v. DHS*, 594 U.S. 758 (2021) (per curiam), the agency had imposed a *new* moratorium on evictions, relying on a longstanding statute that had not been used for that purpose. By contrast, the FDAAA compels FDA to regulate mifepristone.

Appellees cite (at 28) *Utility Air Regulatory Group v. EPA*, 573 U.S. 302, 324 (2014), to assert that the FDAAA cannot preempt the UCPA if it "say[s] nothing about" abortion. But, as the district court

correctly reasoned: (1) "Congress *did* specify that drugs previously approved under Subpart H would be deemed in effect to have a REMS in the 2007 FDAAA"; (2) "[s]hortly thereafter, the FDA issued a notice indicating that mifepristone was one of these previously approved drugs"; and (3) FDA's "list consisted of only 17 previously approved drugs and Congress undoubtedly knew that one, mifepristone, was used only for medication abortion." JA263. The statute addresses abortion by empowering FDA to regulate a drug *whose only indication is abortion*.

D. West Virginia's Counseling And Waiting Period Requirements Are Preempted

West Virginia's counseling and waiting period requirements (which are separate from the UCPA) conflict with mifepristone's safe-use elements. *See* W. Va. Code §16-2I-2. The REMS requires GenBioPro to certify healthcare providers, who must agree to review the REMS Patient Agreement Form with patients before prescribing the drug. This form specifies that patients understand they will take both "mifepristone and misoprostol to end [their] pregnancy."[14]

[14] 2023 Mifepristone REMS, *supra* note 1, at 10.

West Virginia requires providers to communicate the opposite: patients "shall be informed that" they need not take both drugs, as "it may be possible to counteract the intended effects of . . . mifepristone" by abstaining from misoprostol and taking "progesterone." *Id.* § 16-2I-2(a)(4)(A). Appellees argue (at 48) that this requirement "complements" the REMS. But it requires doctors to tell patients information that contradicts the REMS, informing patients they may take only one drug in the two-drug regimen, when the Patient Agreement Form specifies patients understand they will take both. Appellees' bald assertion (at 51) that the information in the UCPA informs women "of the ability to make life-saving choices" is unsupported.

West Virginia's waiting period also conflicts with the REMS. FDA chose not to impose a waiting period for mifepristone, as it has with other drugs.[15] West Virginia's decision to impose one improperly burdens access and the healthcare system.

The Court should address the constitutionality of the waiting period and counseling requirements, which restricted GenBioPro's

[15] *E.g.*, Isotretinoin REMS, *supra* note 3, at 2.

market in West Virginia and remain part of the Code. W. Va. Code § 16-2R-9. The district court correctly held that GenBioPro "may challenge the[se] provisions which would spring back into enforceability if this Court were to find the UCPA unconstitutional." JA110.

Appellees cite (at 48) *California v. Texas*, 593 U.S. 659, 669-71 (2021), to argue GenBioPro cannot challenge these restrictions, but that case involved a provision carrying a penalty of $0 with "no means of enforcement." Here, invalidating the UCPA would revive the challenged restrictions, rendering jurisdiction proper. *See Associated Indem. Corp. v. Fairchild Indus., Inc.*, 961 F.2d 32, 35 (2d Cir. 1992) ("That the liability may be contingent does not necessarily defeat jurisdiction . . . .").

Appellees cite (at 49) *Planned Parenthood of Southeastern Pennsylvania v. Casey*, 505 U.S. 833 (1992), but *Casey* is irrelevant to preemption. It predated the FDAAA, mifepristone's approval, and FDA's determination that no waiting period was appropriate for mifepristone under the statute's burden and access balancing.

II. GENBIOPRO HAS STANDING AND A CAUSE OF ACTION

A. GenBioPro Plausibly Alleged Standing

At the motion-to-dismiss stage, a plaintiff must plausibly allege "(1) an injury in fact, (2) a sufficient causal connection between the injury and the conduct complained of, and (3) a likelihood that the injury will be redressed by a favorable decision." *Susan B. Anthony List v. Driehaus*, 573 U.S. 149, 157-58 (2014) (cleaned up). A plaintiff whose standing has been challenged gets "the same procedural protection" as any other plaintiff opposing a motion to dismiss, *Wikimedia Found. v. NSA*, 857 F.3d 193, 208 (4th Cir. 2017), so the Court must "draw all reasonable inferences in favor of" GenBioPro, *King v. Rubenstein*, 825 F.3d 206, 212 (4th Cir. 2016).

1. GenBioPro plausibly alleged economic injury

GenBioPro plausibly alleged that West Virginia's laws inflicted "financial harm," the "classic and paradigmatic form of injury in fact." *Maryland Shall Issue, Inc. v. Hogan*, 971 F.3d 199, 210 (4th Cir. 2020). GenBioPro worked for nearly a decade to gain FDA approval to market mifepristone and has used that license to sell approximately 850,000 units nationwide. JA299-300, JA315, JA322 (¶¶ 2, 3, 60, 77). The UCPA "constricted the market for mifepristone statewide," JA302

(¶ 11), "mak[ing] it impossible for GenBioPro to promote and market its product in West Virginia as it does in other states," JA322 (¶ 77), and "caus[ing] significant, ongoing economic injury to GenBioPro in the form of lost sales, customers, and revenue," JA322 (¶¶ 78-79).

The district court was right to find "nothing 'conjectural or hypothetical' about GenBioPro's affirmations that it would be selling its product to a wider market in West Virginia were it not for the UCPA." JA105. These "lost business opportunities" and "the operation of a challenged statute that results in the constriction of a vendor's buyers' market plainly inflict[] an injury in fact." *Maryland Shall Issue*, 971 F.3d at 211 (cleaned up).

Appellees misstate the law and draw inferences against GenBioPro. They argue (at 20) that GenBioPro did not allege *past* sales in West Virginia. But the court rightly noted — and Appellees nowhere acknowledge — that economic injury suffices even if "plaintiffs were not already operating in the targeted market." JA104 (citing *Ezell v. City of Chi.*, 651 F.3d 684, 692, 696 (7th Cir. 2011), and *303 Creative LLC v. Elenis*, 6 F.4th 1160, 1172 (10th Cir. 2021)). Lost future sales are enough for standing. Indeed, GenBioPro intends to sell mifepristone in

West Virginia in the future; that is why it brought this case. JA321-323 (¶¶ 76-80).

Even if past sales were required, GenBioPro alleged them. West Virginia's laws have cost the company "sales, customers, and revenue." JA322 (¶ 79), and GenBioPro's "only revenue producing products are medication abortion drugs," JA105. The only plausible inference is that the company *has sold* mifepristone in West Virginia.[16]

Appellees incorrectly claim (at 20-21) that GenBioPro's failure to allege it certified healthcare providers and pharmacies to prescribe and dispense mifepristone in West Virginia is relevant to standing.[17] But GenBioPro alleged that providers and pharmacies would prescribe and dispense mifepristone were it not for the UCPA. JA323 (¶ 80). GenBioPro will certify them when the UCPA is enjoined as unconstitutional — standing does not require the company to certify providers to prescribe a drug they are banned from selling.

[16] At a hearing, GenBioPro's counsel represented that "there have been past sales by GenBioPro of mifepristone in West Virginia." JA127.

[17] *See* 2023 Mifepristone REMS, *supra* note 1, at 6-9, 11-13.

Appellees suggest (at 21 & n.15) GenBioPro needed a manufacturer's license from West Virginia's Board of Pharmacy. But State rules require such licensing only for "manufacturing of prescription drugs in this state," W. Va. Code § 15-5-3.2, and GenBioPro's mifepristone is manufactured elsewhere.

2. GenBioPro plausibly alleged a credible threat of prosecution

A plaintiff independently pleads injury if it alleges "an intention to engage in a course of conduct arguably affected with a constitutional interest, but proscribed by a statute, and there exists a credible threat of prosecution thereunder." *Susan B. Anthony*, 573 U.S. at 159.

GenBioPro's intended sales raise a constitutional interest because West Virginia's restrictions violate the Supremacy Clause. *See supra* pp. 3-27. Unrebutted allegations show the threat of prosecution is credible. Appellee Morrisey, West Virginia's Attorney General, "has responsibility for enforcing the laws of West Virginia" and intends to enforce the UCPA "notwithstanding FDA's determinations pursuant to its congressional mandate." JA305-306 (¶ 25). Appellee Raynes, Putnam County's Prosecuting Attorney, "has authority to prosecute violations of the [UCPA] and other criminal restrictions on abortion in

Putnam County," and has said that "[a]s prosecutors we have a clear obligation to enforce the laws of our state," including against "medical provider[s]" providing abortion services. JA305 (¶ 24); *see supra* pp. 14-15.

Appellees argue (at 21-22) that the UCPA does not prohibit GenBioPro's sales because mifepristone may be used off-label or in the law's few "exceptions," such as incest. But FDA approved GenBioPro's mifepristone *only* for abortion, no matter the cause of pregnancy. JA314 (¶ 58). West Virginia forbids providing mifepristone for that purpose. *See supra* pp. 9-10. GenBioPro's exposure to prosecution and the credible threats of enforcement confer standing.[18]

3. GenBioPro plausibly alleged third-party standing

GenBioPro has standing on behalf of the healthcare providers and pharmacies that would prescribe and dispense mifepristone but for West Virginia's restrictions. "[A] vendor has a sufficiently close

[18] Appellees do not dispute that GenBioPro's injury is fairly traceable to the UCPA and redressable with the requested relief. Declaring the UCPA unconstitutional and enjoining its enforcement will lift the restrictions that constrain GenBioPro from providing its product in West Virginia and harm it economically, redressing GenBioPro's injury. *See Maryland Shall Issue*, 971 F.3d at 213.

relationship with its customers" to challenge a law on their behalf "when a challenged statute prevents that entity from transacting business with them." *Maryland Shall Issue*, 971 F.3d at 216. As the district court held, "GenBioPro may assert the third-party rights" of its vendees — healthcare providers and pharmacies — "who seek access to its market but are prevented by the UCPA from transacting business with GenBioPro." JA114. Appellees' only counterargument (at 22-23), that GenBioPro may not assert *third-party* standing because it lacks *first-party* standing, fails for the reasons discussed above.

B. Appellees Forfeited Their Cause-Of-Action Defense, Which Lacks Merit

1. Appellees forfeited any cause-of-action defense

Appellees forfeited their argument (at 23-26) that GenBioPro has no cause of action to challenge West Virginia's laws because Appellees failed to raise it below. Whether a plaintiff has a cause of action "is not a question of jurisdiction," and is subject to forfeiture. *Air Courier Conf. of Am. v. American Postal Workers Union, AFL-CIO*, 498 U.S. 517, 523 n.3 (1991). A party forfeits a cause-of-action defense by failing to raise it first in the district court. *See Remy Holdings Int'l, LLC v. Fisher Auto Parts, Inc.*, 90 F.4th 217, 231 n.11 (4th Cir. 2024). Thus, in *Hicks*

v. Ferreyra, 965 F.3d 302, 309-10 (4th Cir. 2020), this Court found forfeiture because the defendants did not "argue or even suggest that [plaintiff] lacked a cause of action" in district court.

The Court should hold Appellees to their forfeiture. They cite cases (at 25-26) to the effect that the Court may affirm for any reason apparent in the record, but none supports the argument that a court should consider a forfeited argument. Courts consider an argument for the first time on appeal only in "exceptional circumstances," *Williams v. Kincaid*, 45 F.4th 759, 776 (4th Cir. 2022), in which "the newly raised argument establishes 'fundamental error' or a denial of fundamental justice," *Hicks*, 965 F.3d at 310.

This case presents no such circumstances. Appellees do not argue fundamental error or that it would deny fundamental justice to decline to address their belated cause-of-action defense. So they have abandoned the opportunity to have this new argument considered on appeal. *See In re Under Seal*, 749 F.3d 276, 292 (4th Cir. 2014).

2. *Ex parte Young* provides a cause of action in equity

Even if the Court were to reach the issue, GenBioPro has an equitable cause of action under *Ex parte Young*, 209 U.S. 123 (1908),

which empowers the company "to petition a federal court to enjoin State officials . . . from engaging in future conduct that would violate the Constitution." *Antrican v. Odom*, 290 F.3d 178, 184 (4th Cir. 2002). A plaintiff bringing such an action must allege "an ongoing violation of federal law" and seek "prospective" relief. *Franks v. Ross*, 313 F.3d 184, 197 (4th Cir. 2002) (quoting *Verizon Md. Inc. v. Public Serv. Comm'n*, 535 U.S. 635, 645 (2002)). Plaintiffs plead a valid cause of action by alleging that a state official would violate the Supremacy Clause by enforcing a preempted state law. *See, e.g.*, *United States v. South Carolina*, 720 F.3d 518, 525-26 (4th Cir. 2013).

GenBioPro seeks prospective relief against state officials with the power and intent to enforce West Virginia's unconstitutional laws. *See* JA305-306, JA326-331. GenBioPro plausibly alleged — and Appellees do not contest — a credible threat that these officials will enforce those unconstitutional restrictions on access to mifepristone. *Supra* pp. 30-31. GenBioPro has a cause of action to enjoin that enforcement.

Appellees rely on *Armstrong v. Exceptional Child Center, Inc.*, 575 U.S. 320, 326 (2015), to argue that equity does not provide a basis for this lawsuit. Opp. 23-24. *Armstrong* says the opposite: while there

is no "implied right of action contained in the Supremacy Clause," equity confers a right "to sue to enjoin unconstitutional actions by state and federal officers." 575 U.S. at 327.

Appellees' reference (at 24-25) to a bar on private FDCA "enforcement suits" is irrelevant; this is not an enforcement suit. GenBioPro alleges that "federal law immunizes [it] from state regulation" — Appellees' unconstitutional enforcement of West Virginia's laws. *Armstrong*, 575 U.S. at 326. GenBioPro has a valid cause of action in equity, and "the court may issue an injunction upon finding the state regulatory actions preempted." *Id*.

CONCLUSION

The district court's judgment should be reversed.

May 20, 2024

Respectfully submitted,

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UNITED STATES COURT OF APPEALS FOR THE FOURTH CIRCUIT

No. 23-2194 **Caption:** GenBioPro, Inc. v. Kristina Raynes et al.

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(s) David C. Frederick

Party Name GenBioPro, Inc.

Dated: May 20, 2024

CERTIFICATE OF SERVICE

I hereby certify that, on May 20, 2024, I electronically filed the foregoing Reply Brief for Plaintiff-Appellant GenBioPro, Inc., with the Clerk of the Court for the United States Court of Appeals for the Fourth Circuit using the appellate CM/ECF system.

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