No. 23-10362

IN THE UNITED STATES COURT OF APPEALS FOR THE FIFTH CIRCUIT

ALLIANCE FOR HIPPOCRATIC MEDICINE; AMERICAN ASSOCIATION OF PRO-LIFE OBSTETRICIANS & GYNECOLOGISTS; AMERICAN COLLEGE OF PEDIATRICIANS; CHRISTIAN MEDICAL & DENTAL ASSOCIATIONS; SHAUN JESTER, D.O.; REGINA FROST-CLARK, M.D.; TYLER JOHNSON, D.O.; GEORGE DELGADO, M.D.,

Plaintiffs-Appellees,

v.

U.S. FOOD & DRUG ADMINISTRATION; ROBERT M. CALIFF, Commissioner of Food and Drugs; JANET WOODCOCK, M.D., in her official capacity as Principal Deputy Commissioner, U.S. Food and Drug Administration; PATRIZIA CAVAZZONI, M.D., in her official capacity as Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; XAVIER BECERRA, Secretary, U.S. Department of Health and Human Services,

Defendants-Appellants,

v.

DANCO LABORATORIES, L.L.C.,

Intervenor-Appellant.

On Appeal from the United States District Court
for the Northern District of Texas

BRIEF FOR FEDERAL APPELLANTS

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CERTIFICATE OF INTERESTED PERSONS

Alliance for Hippocratic Medicine, et al. v. U.S. Food & Drug Administration, et al.

The undersigned counsel of record certifies that the following listed persons and entities as described in the fourth sentence of Rule 28.2.1 have an interest in the outcome of this case. These representations are made in order that the judges of this court may evaluate possible disqualification or recusal.

Plaintiffs-Appellees:

Alliance for Hippocratic Medicine

American Association of Pro-Life Obstetricians & Gynecologists

American College of Pediatricians

Christian Medical & Dental Associations

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Defendants-Appellants:

U.S. Food and Drug Administration

U.S. Department of Health and Human Services

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STATEMENT REGARDING ORAL ARGUMENT

Oral argument has been scheduled for May 17, 2023. This case presents substantial legal questions that profoundly affect the Food and Drug Administration's authority to regulate drugs, the lives of millions of women who depend on access to mifepristone, and many others. Oral argument is necessary for full consideration of these issues.

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Cases: **Page(s)**

Statutes:

Regulations:

Legislative Materials:

Other Authorities:

INTRODUCTION

This is an appeal from an unprecedented order countermanding the scientific judgment of the Food and Drug Administration (FDA) by suspending the agency's approval of mifepristone. In 2000, FDA approved mifepristone as safe and effective for termination of early pregnancy. FDA has maintained that scientific judgment across five presidential administrations. Public health authorities around the world likewise have approved mifepristone, and the World Health Organization has declared it to be an "Essential Medicine." ROA.2154. More than five million Americans have ended their pregnancies using the drug. Today, more than half of women in this country who choose to terminate their pregnancies rely on mifepristone to do so. And study after study has shown that when mifepristone is taken consistent with its approved conditions of use, serious adverse events are "exceedingly rare." ROA.2189.

In a sweeping order, the district court invoked 5 U.S.C. § 705 to suspend FDA's 2000 approval of mifepristone and a series of subsequent FDA actions modifying the drug's approved conditions of use. Like all preliminary relief, a § 705 order is supposed to "preserve

status or rights" pending review. 5 U.S.C. § 705. But the district court's order would do exactly the opposite: By nullifying FDA's approval, the order would upend the status quo based on the court's deeply misguided assessment of mifepristone's safety. And the court took that extraordinary step even though plaintiffs' own conduct belies any need for extraordinary relief: They did not sue until more than two decades after mifepristone's approval, delayed three years before petitioning FDA to reconsider its 2016 action, waited nearly a year to sue after FDA denied that petition, and then unsuccessfully urged the district court to defer consideration of preliminary relief until after a trial on the merits.

To the government's knowledge, this is the first time any court has abrogated FDA's approval of a drug based on disagreement with the agency's judgment about safety—much less done so after that approval has been in effect for decades. The district court reached that unprecedented result only through a series of fundamental errors that violate bedrock Article III and administrative law principles. Plaintiffs lack standing under controlling Supreme Court precedent; their central

challenge is untimely; and none of their claims has any basis in the Federal Food, Drug, and Cosmetic Act (FDCA).

Finally, the overwhelmingly one-sided balance of the equities by itself should have precluded the abrupt and profoundly disruptive nationwide relief granted below. The district court's order would thwart FDA's scientific judgment and profoundly harm women who rely on mifepristone as an alternative to more burdensome and invasive surgical abortions. Those harms would be felt throughout the Nation because mifepristone has lawful uses in every State—even those with restrictive abortion laws. And the district court's order is damaging to healthcare providers and drug sponsors, who also rely on FDA's scientific judgment and orderly administration of the Nation's complex system of drug regulation. In contrast, plaintiffs have not shown that they will be injured at all, much less irreparably, by maintaining the status quo that they left unchallenged for years and that the Supreme Court has now preserved during these proceedings.

STATEMENT OF JURISDICTION

Plaintiffs invoked the district court's jurisdiction under 28 U.S.C. § 1331 and moved for a preliminary injunction. On April 7, 2023, the

court granted that motion in part and, invoking 5 U.S.C. § 705, stayed the effective date of several agency actions. The government filed a notice of appeal the same day. This Court stayed the district court's order in part on April 12, 2023, and the Supreme Court stayed the district court's order in full on April 21, 2023. This Court has jurisdiction under 28 U.S.C. § 1292(a)(1). ROA.4385 n.3.

STATEMENT OF THE ISSUES

1. Whether plaintiffs' claims are judicially reviewable.

2. Whether FDA's challenged actions were lawful.

3. Whether the equities further demonstrate that the district court abused its discretion.

STATEMENT OF THE CASE

A. Statutory And Regulatory Background

Congress has entrusted FDA with the authority and responsibility to ensure that "new drug[s]" are safe and effective. 21 U.S.C. §§ 321(p), 355, 393(b)(2)(B). The FDCA directs the agency to approve a new drug application if, among other things, it contains evidence demonstrating that the drug is safe and effective for its intended use. *Id.* § 355(d); 21 C.F.R. §§ 314.50, 314.105(c).

In 1992, FDA issued regulations providing for the imposition of conditions "needed to assure safe use" of certain new drugs that satisfy the other requirements for approval under the FDCA. 57 Fed. Reg. 58,942, 58,948 (Dec. 11, 1992) (21 C.F.R. § 314.520). Those "Subpart H" regulations apply to certain new drugs that are used to treat "serious or life-threatening illnesses" and that provide "meaningful therapeutic benefit to patients over existing treatments." 21 C.F.R. § 314.500.

In 2007, Congress codified and expanded on the authority exercised by FDA through Subpart H by authorizing the agency to require a "risk evaluation and mitigation strategy" (REMS) when it determines that such a strategy is necessary to ensure that the benefits of a drug outweigh the risks. 21 U.S.C. § 355-1; Food and Drug Administration Amendments Act of 2007 (FDAAA), Pub. L. No. 110-85, tit. IX, § 901, 121 Stat. 823, 922-43. Under the REMS framework, a drug approval may include "elements to assure safe use," such as a requirement that a drug's prescribers have particular training or that a drug be dispensed only in certain settings. 21 U.S.C. § 355-1(f)(3). FDA may modify an approved REMS if it determines that new requirements

are needed to assure safe use or that existing requirements are no longer necessary. *Id.* § 355-1(g), (h).

B. FDA's Actions Addressing Mifepristone

1. In 2000, after a four-year review of the original sponsor's application, FDA approved mifepristone under the brand name Mifeprex. ROA.591-98. Mifepristone is approved for use with another drug, misoprostol, to end an early pregnancy. A patient who follows the two-drug regimen experiences cramping and bleeding similar to a miscarriage. ROA.2209-11. In approving mifepristone, FDA invoked its Subpart H regulations to impose requirements to assure the drug's safe use, including a requirement that mifepristone be dispensed in person by or under the supervision of a doctor with specified qualifications. ROA.596. FDA concluded based on a review of clinical trials and other scientific evidence that, under those conditions, mifepristone was safe and effective to terminate pregnancy through seven weeks of gestation. ROA.591-98.

When Congress adopted the REMS framework in 2007, it deemed drugs with existing Subpart H restrictions—which included mifepristone—to have an approved REMS imposing the same

restrictions. FDAAA § 909(b), 121 Stat. at 950-51 (21 U.S.C. § 331 note). Since then, the REMS framework has governed mifepristone's distribution restrictions. FDA first approved the REMS for mifepristone in 2011, including similar restrictions as in 2000. ROA.672; ROA.677-81; ROA.804.

2. In 2016, FDA approved an application from mifepristone's sponsor, intervenor-appellant Danco Laboratories, LLC, that sought to alter the drug's conditions of use (including the REMS). ROA.689-94. FDA's approval followed a comprehensive review of the proposed modifications that considered "20 years of experience with [mifepristone], guidelines from professional organizations here and abroad, and clinical trials that have been published in the peer-reviewed medical literature." ROA.2159; *see* ROA.2143-2242. Three aspects of FDA's 2016 action are relevant here.

First, FDA changed mifepristone's conditions of use. Relying on safety and efficacy data from nearly two dozen studies, FDA increased the gestational age limit from seven to 10 weeks. ROA.2171-80; ROA.712-13. Relying on additional studies, FDA also reduced the number of required in-person clinical visits from three to one.

ROA.2180-83; ROA.2206-09; ROA.713-14. And FDA allowed certified healthcare providers licensed to prescribe drugs under state law (rather than only physicians) to prescribe and dispense mifepristone. ROA.2185-86; ROA.713-15. The agency concluded that the revised conditions of use would ensure mifepristone's safety, emphasizing that major adverse events "are exceedingly rare." ROA.2189.

Second, FDA changed the approved dosing regimen. ROA.2148. For example, FDA reduced the amount of mifepristone from 600 mg to 200 mg, increased the amount of misoprostol, and changed the route of administration of the misoprostol from oral to buccal (dissolved in the cheek pouch). ROA.2148. Plaintiffs have not challenged those changes in this litigation, and neither the district court nor this Court during stay proceedings suggested they were unlawful.

Third, FDA modified a prior requirement that, in the Prescriber Agreement Form, prescribers agree to report certain serious adverse events such as blood transfusions to the drug's sponsor. ROA.724. FDA concluded based on over "15 years of reporting" that the requirement could be narrowed and that, as with other prescription drugs, information on non-fatal adverse events would continue to be "collected

in the periodic safety update reports and annual reports" submitted by the sponsor to FDA. ROA.724.

3. In 2019, FDA approved an application of another sponsor, GenBioPro, Inc., to market a generic version of mifepristone based on FDA's determination that it was therapeutically equivalent to Mifeprex. ROA.768; *see* 21 U.S.C. § 355(j). The same REMS covers both versions of mifepristone. ROA.768-69.

4. In April 2021, FDA announced that it would exercise enforcement discretion during the COVID-19 public health emergency with respect to the in-person dispensing requirement. ROA.807. FDA explained that its decision "was the result of a thorough scientific review by experts" who evaluated evidence including "clinical outcomes data and adverse event reports." ROA.807.

C. Plaintiffs' Citizen Petitions

Before filing a suit challenging FDA's decisions, a party generally must file a citizen petition with FDA. 21 C.F.R. § 10.45(b). Plaintiffs filed two citizen petitions relevant here.

In 2002, two plaintiffs filed a petition asking FDA to withdraw its 2000 approval of mifepristone. ROA.635. FDA denied that petition in

March 2016, on the same day it approved modifications to mifepristone's conditions of use. ROA.635-67. FDA explained that "adequate and well-controlled clinical trials" had "supported the safety of Mifeprex" in 2000 and that "over 15 years of postmarketing data and many comparative clinical trials in the United States and elsewhere continue to support [its] safety." ROA.651. FDA also explained that it had properly approved mifepristone under its Subpart H regulations, noting that "[p]regnancy can be a serious medical condition in some women" and 92% of women in the phase 3 clinical trial of Mifeprex "avoided an invasive surgical procedure and anesthesia." ROA.637-41.

In 2019, two plaintiffs filed a petition challenging FDA's 2016 changes to mifepristone's conditions of use. ROA.741. That petition did not ask FDA to revisit the 2000 approval; instead, it asked FDA to "restore" the 2000 conditions and "retain" the REMS, including the in-person dispensing requirement. ROA.741. In December 2021, FDA denied that petition in relevant part. ROA.803-42. FDA explained that none of plaintiffs' cited studies undermined FDA's findings from 2016. ROA.809-23. FDA also concluded based on its extensive review of the scientific evidence that "mifepristone may be safely used without in-

person dispensing." ROA.829-38. FDA thus directed mifepristone's sponsors to submit a proposed REMS modification with that change, among others. ROA.808-09; *see* 21 U.S.C. § 355-1(g)(4)(B). In 2023, after this suit was filed, FDA approved the removal of the in-person dispensing requirement from the REMS. FDA, *REMS Single Shared System for Mifepristone 200 mg* (Jan. 2023), https://perma.cc/MJT5-35LF.[1]

D. Prior Proceedings

1. Plaintiffs are individual physicians and organizations representing physicians. In November 2022, they filed this suit to challenge six FDA actions spanning more than 20 years: the 2000 approval of Mifeprex; the 2016 changes to the conditions of use; the 2019 approval of generic mifepristone; the 2021 exercise of enforcement discretion; and the 2016 and 2021 responses to plaintiffs' citizen petitions. ROA.167-83. Plaintiffs sought a preliminary injunction to suspend all of those actions. ROA.183-84.

[1] Plaintiffs did not challenge FDA's 2023 action, and the district court did not discuss it.

The district court directed the parties to submit briefs "on whether the Court should consolidate the injunction hearing and the trial on the merits." ROA.2521. Plaintiffs urged the court to defer ruling on their preliminary injunction motion until after production of the administrative record and a trial on the merits, ROA.3246-51, but the court ultimately declined that request to delay consideration of preliminary relief, ROA.4192.

2. On April 7, 2023, the district court granted plaintiffs' motion for preliminary relief. The court rejected the government's arguments that plaintiffs' claims are not judicially reviewable. On the merits, the court held that FDA's actions were arbitrary and capricious, largely based on the court's own interpretation of extra-record publications. ROA.4355-66. The court also held that FDA's 2000 approval of mifepristone improperly relied on Subpart H of FDA's regulations, ROA.4345-54, and that statutory provisions derived from the 1873 Comstock Act prohibited FDA from removing the in-person dispensing requirement, ROA.4338-44; *see* 18 U.S.C. §§ 1461, 1462. Finally, the court determined that the equities and public interest favored relief. ROA.4367-71.

Although plaintiffs' motion sought a preliminary injunction, the district court instead invoked 5 U.S.C. § 705 to "stay" the effective date of "FDA's September 28, 2000 Approval of mifepristone and all subsequent challenged actions," even though the effective date of those actions had passed years earlier. ROA.4371-73. The court then stayed its own order for seven days to allow the government to seek emergency relief from this Court. ROA.4373.[2]

3. On April 10, the government and Danco sought stays pending appeal. On April 12, a divided panel of this Court granted a stay in part and denied it in part. The panel majority stayed the district court's decision with respect to FDA's approval of mifepristone in 2000, holding that the challenge was likely time-barred and that the equities favored defendants on that claim. ROA.4400-07, 4417. The panel majority denied a stay with respect to FDA's other challenged actions. ROA.4419.

[2] Shortly after the district court issued its order, another district court enjoined FDA from "altering the status quo" with respect to mifepristone's availability in certain States. Order, *Washington v. FDA*, No. 23-3026 (E.D. Wash. Apr. 7, 2023), ECF No. 80.

On April 21, the Supreme Court stayed the district court's order in full pending appeal.

SUMMARY OF ARGUMENT

I. Plaintiffs' claims are not judicially reviewable. Plaintiffs lack Article III standing under controlling Supreme Court precedent. Plaintiffs are doctors and associations of doctors who oppose abortion. They neither take nor prescribe mifepristone, and FDA's approval of the drug does not require them to do or refrain from doing anything. Yet the district court held that the associations have standing because some of their members might be asked to treat women who are prescribed mifepristone by other providers and who then suffer an exceedingly rare serious adverse event. The Supreme Court has squarely rejected that statistical approach to associational standing, explaining that it would "make a mockery" of Article III. *Summers v. Earth Island Inst.*, 555 U.S. 488, 498 (2009). That theory also rests on the false premise that mifepristone is unsafe under the approved conditions of use; in reality, serious adverse events are exceedingly rare. In any event, standing is not dispensed in gross; plaintiffs utterly fail to demonstrate any injury

to support their claims challenging FDA's actions in 2016 and thereafter.

Plaintiffs also lack organizational standing and third-party standing. The plaintiff organizations have not suffered any Article III injury from FDA's changes to the reporting requirements applicable only to third parties. Nor can plaintiffs assert third-party standing on behalf of hypothetical future patients who might someday use mifepristone. Plaintiffs' interests are diametrically opposed to those patients who, by definition, want to use mifepristone. In any event, plaintiffs are outside the zone of interests of any relevant statute.

Finally, plaintiffs' challenge to the 2000 approval of mifepristone is time-barred by the six-year statute of limitations. FDA approved mifepristone in 2000 and denied plaintiffs' citizen petition challenging that approval in March 2016. Plaintiffs waited more than six years after those decisions to file their complaint. None of FDA's later actions restarted the statute of limitations by reopening the original approval. Nor are plaintiffs entitled to equitable tolling, given that nothing prevented them from filing suit within the limitations period.

II. Plaintiffs' challenges also fail on the merits. FDA's actions were amply supported by a record developed over decades of safe and effective use of mifepristone in the United States and around the world. While FDA justified its scientific conclusions in multiple detailed reviews, including a medical review spanning more than 100 pages and assessing dozens of studies and other scientific information, the district court swept the agency's judgments aside by substituting its own lay understanding of purportedly contrary studies, offering demonstrably erroneous characterizations of the record.

FDA's 2000 approval of mifepristone was lawful. FDA reasonably explained its decision, relying on multiple clinical trials that demonstrated the drug's safety and efficacy. The district court overturned FDA's decision because the agency relied on studies with somewhat different protocols than the approved conditions of use. But the court's apparent "study match" requirement has no basis in the FDCA or administrative law. The court also concluded that FDA's original approval was invalid under the agency's Subpart H regulations, but FDA's decision complied with those regulations, and, in any event, mifepristone is now regulated under the statutory REMS framework.

FDA's remaining actions were likewise lawful. In 2016, FDA reasonably approved changes to mifepristone's conditions of use (including the REMS), relying on an exhaustive review of decades of data, published literature, and other evidence. FDA also reasonably changed (but did not eliminate) the adverse event reporting requirements for prescribers under the REMS, determining that over 15 years of reporting data had firmly established mifepristone's "well-characterized safety profile." ROA.822. Additionally, FDA properly approved generic mifepristone in 2019 as therapeutically equivalent to the branded version. Finally, relying on a thorough scientific review, FDA reasonably decided to remove the in-person dispensing requirement. Contrary to the district court's conclusion, the Comstock Act did not prevent FDA from removing that requirement. The FDCA does not require the agency to address separate criminal statutes when it approves a drug or imposes a REMS. Regardless, the Comstock Act does not prohibit the mailing of abortion drugs intended for lawful use.

III. The district court also contravened established equitable principles in granting preliminary relief. The court's reliance on 5 U.S.C. § 705 was misplaced for multiple reasons. The equities also

independently foreclose preliminary relief. The purpose of preliminary relief is to preserve the status quo, yet the district court's order upends the status quo that has been in effect for over two decades. That decision severely harms women, the Nation's healthcare system, FDA, and the public interest generally. In contrast, plaintiffs would not be harmed without preliminary relief. Their harms are attenuated, speculative, and do not remotely justify upending the status quo. Plaintiffs' own delay in bringing suit underscores their lack of urgency.

STANDARD OF REVIEW

This Court reviews a stay decision under 5 U.S.C. § 705 for abuse of discretion. *See Cronin v. USDA*, 919 F.2d 439, 446 (7th Cir. 1990) (the standard to grant a preliminary injunction or a stay under § 705 is "the same"); *Planned Parenthood of Greater Tex. Family Planning & Preventative Health Servs., Inc. v. Kauffman*, 981 F.3d 347, 354 (5th Cir. 2020) (en banc) (preliminary injunction reviewed for abuse of discretion). "When a district court applies incorrect legal principles, it abuses its discretion." *Kauffman*, 981 F.3d at 354.

ARGUMENT

I. Plaintiffs' Claims Are Not Judicially Reviewable

A. Plaintiffs Lack Article III Standing

Under Article III, a plaintiff must show injury in fact, causation, and redressability. *TransUnion LLC v. Ramirez*, 141 S. Ct. 2190, 2203 (2021). To establish injury in fact, plaintiffs must show "an invasion of a legally protected interest" that is both "concrete and particularized" and "actual or imminent, not conjectural or hypothetical." *Spokeo, Inc. v. Robins*, 578 U.S 330, 339 (2016). Thus, "'allegations of *possible* future injury' are not sufficient." *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 409 (2013).

1. Plaintiffs Lack Associational Standing

a. The district court erred in holding that plaintiff-associations have standing to assert the interests of their physician-members. ROA.4313-15. Plaintiffs and their members oppose abortion and therefore oppose the use of mifepristone. But plaintiffs and their members (hereafter plaintiffs or plaintiff doctors) "are not required to receive" or prescribe mifepristone, and "[t]hey do not have standing to challenge FDA's decision to allow *other people* to receive" or prescribe the drug because that decision does not impose any concrete,

particularized, or imminent harm on plaintiffs. *Coalition for Mercury-Free Drugs v. Sebelius*, 671 F.3d 1275, 1277 (D.C. Cir. 2012) (Kavanaugh, J.). "The Constitution therefore requires that [plaintiffs] direct their objections to the Executive and Legislative Branches, not to the Judiciary." *Id.* at 1283.

The district court nevertheless held that plaintiffs have standing on the theory that *other* providers will prescribe mifepristone to patients after informing them of its risks and benefits; that some small fraction of those patients will experience exceedingly rare serious adverse events; that some subset of that small fraction of women (who by definition chose to terminate their pregnancies) will then seek care from the plaintiff doctors who are opposed to abortion and with whom they lack any prior relationship; and that those women will do so in sufficient numbers to burden those doctors' medical practices or will require treatment by a plaintiff doctor who morally objects to providing treatment. ROA.4313-14.

To describe that theory is to refute it. The Supreme Court has repeatedly rejected theories of standing that rest on a "speculative chain of possibilities," *Clapper*, 568 U.S. at 414, especially where, as

here, those possibilities depend on "unfettered choices made by independent actors," *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 562 (1992). In *Clapper*, for example, the Court reversed a decision finding standing based on "an objectively reasonable likelihood" that the named plaintiffs would suffer injury from the challenged policy. 568 U.S. at 410. The Court emphatically rejected that probabilistic approach as "inconsistent with [the] requirement that 'threatened injury must be certainly impending.'" *Id.*; *see E.T. v. Paxton*, 41 F.4th 709, 714-16 (5th Cir. 2022). So too here.

The court relied heavily on plaintiffs' allegation that some of the plaintiff doctors have treated patients for complications from mifepristone in the past. ROA.4320. But even though mifepristone has been taken by more than five million women in America and the plaintiff organizations claim to have thousands of members practicing around the country, ROA.81-83, they allege only sporadic incidents, none of which meaningfully interfered with a member's medical practice. *See* ROA.269-70; ROA.278-83; ROA.290-91; ROA.296-97; ROA.959. And—even assuming that treating a patient qualifies as a legally cognizable Article III injury to a doctor—standing to seek

prospective relief cannot be based on such "past injury"; instead, plaintiffs must show an "imminent future injury" to one or more *identified* physicians. *Summers v. Earth Island Inst.*, 555 U.S. 488, 495 (2009).

Plaintiffs have not done so. Instead, their theory mirrors the "hitherto unheard-of test" for standing that the Supreme Court flatly rejected in *Summers*, 555 U.S. at 497. There, an environmental association challenged regulations facilitating timber-salvage projects. At least one member had been harmed by a past project, and the association claimed its members would be harmed by projects in the future. *Id.* at 495. The Court held, however, that such past harm "does not suffice" to show standing "because it relates to past injury rather than imminent future injury that is sought to be enjoined." *Id.* at 495-96. It "would make a mockery" of Article III to find associational standing wherever, based on an "organization's self-description of the activities of its members, there is a statistical probability that some of those members are threatened with concrete injury." *Id.* at 497-98. The Court emphasized that an organization must "make specific allegations establishing that at least one *identified* member" will suffer harm, a

requirement that "has never been dispensed with in light of statistical probabilities." *Id.* at 498-99 (emphasis added). The district court engaged in precisely that type of prohibited statistical approach when it reasoned that plaintiffs have "good reasons to believe" some unknown members will treat patients for mifepristone complications in the future. ROA.4321.

Beyond that flat inconsistency with *Summers*, plaintiffs offer no limiting principle for their boundless theory of standing. Under their approach, associations of doctors could sue to challenge any government action that might affect a member's practice. Pulmonologists could sue the Environmental Protection Agency to challenge regulations that increased (or reduced) air pollution; pediatricians could sue the Department of Agriculture to challenge standards that imperiled (or improved) student nutrition; and emergency room doctors could sue the government to challenge regulations that loosened (or restricted) access to firearms. Similarly, were the "stress" that doctors feel when they treat patients a cognizable Article III injury, ROA.4313, doctors would have standing to sue a multitude of manufacturers and regulators; surely some find it stressful to treat gun-shot victims, drunk drivers, or

individuals experiencing an opioid overdose. Plaintiffs' extravagant concept of injury is not the law.

b. Moreover, plaintiffs' theory of standing rests on the false premise that mifepristone is unsafe under the approved conditions of use. The stay panel accepted that premise, reasoning that the "record" demonstrates that "hundreds of thousands of women *will* … need emergency care" after using mifepristone, and "plaintiff doctors and their associations will necessarily be injured by the consequences." ROA.4396. Under *Summers*, those assertions would not establish Article III injury even if they were correct. But they are incorrect.

Serious adverse events associated with mifepristone are "exceedingly rare." ROA.2189. The mifepristone labeling indicates, for example, that sepsis and hemorrhage rates are each 0.2% or less and that rates of transfusion and hospitalization related to medication abortion are each 0.7% or less. *See Mifepristone Labeling* 8, https://perma.cc/PU3Y-7TSK; *see also* ROA.708-09. The rate of emergency room presentation is likewise low. *See* ROA.2189, 2192, 2197-98; ROA.839-40.

The stay panel misread the Patient Agreement Form to indicate a higher rate of adverse events, relying on paragraph 6 to "prove that emergency room care is statistically certain in hundreds of thousands of cases" and that plaintiff doctors are "statistically certain" to provide emergency care in the future. ROA.4398-99; ROA.4389-90. But paragraph 6 states that for 2% to 7% of women, "the treatment will not work," *i.e.*, that it will not be *effective* in completely terminating their pregnancies. ROA.4389. The patient signing the Form agrees in that event to "talk with [her] provider"—who would not be one of plaintiffs' members, who do not prescribe mifepristone—"about a surgical procedure to end [her] pregnancy." ROA.4389. That paragraph does not address "emergency care" at all.[3]

The subject of "emergency care" is instead addressed in paragraph 4, which identifies symptoms that "could require emergency care," and states that the patient agrees to contact her "provider" or another person her "provider has told [her] … to call" in that instance.

[3] An "unsuccessful" treatment will not always require a surgical procedure in an operating room. As FDA explained, "options that are now commonly available include" "expectant management (wait and see)" and "additional doses of misoprostol," among others. ROA.715.

ROA.4389.[4] Similarly, all prescribers of mifepristone must either have the "[a]bility to provide surgical intervention" where necessary or "ma[k]e plans to provide such care through others." *Mifepristone Prescriber Agreement Form* 1, https://perma.cc/MJT5-35LF. There is no reason to assume that women in need of rare emergency care would ignore the plans put in place by their providers and go to a hospital where one of plaintiffs' members happens to be working at the time. *See, e.g.*, ROA.814 (explanation from FDA about common referral practice); ROA.2476-77 (describing practice of doctors to provide "after-hours care" at outpatient abortion clinics). And even if they did, there is no basis to assume that any particular member would be compelled to assist in a procedure contrary to his beliefs. *See* 42 U.S.C. §§ 238n, 300a-7(c), (d) (federal conscience protections); Consolidated Appropriations Act, 2022, Pub. L. No. 117-103, div. H., tit. V, §§ 506-507, 136 Stat. 49, 496 (similar).

[4] The stay panel also relied on the "Black Box" warning for mifepristone, but that warning states that "[s]erious and sometimes fatal infections and bleeding occur very rarely following" miscarriage, surgical abortion, and medication abortion—and that "[n]o causal relationship between the use of [mifepristone] and misoprostol and these events has been established." ROA.4398.

c. In any event, "plaintiffs must demonstrate standing for each claim that they press and for each form of relief that they seek." *TransUnion*, 141 S. Ct. at 2208. The district court (and the stay panel) found standing on the ground that plaintiffs are injured by the availability of mifepristone as a general matter. ROA.4313-14; ROA.4389-90 (counting every adverse event in its statistical analysis). But even if plaintiffs' theory of standing were not speculative and foreclosed by Supreme Court precedent, that asserted injury would at most support plaintiffs' standing to challenge mifepristone's approval in 2000. As discussed below, that challenge is time-barred.

Plaintiffs' other challenges concern FDA's subsequent changes to the conditions of approval, and plaintiffs have not shown that one of their members faces imminent and legally cognizable injury from those particular changes. The district court did not even purport to find that plaintiffs' alleged injuries are "fairly traceable" to FDA's post-approval actions or that relief targeted to those actions would alleviate those injuries. *See Friends of the Earth Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.*, 528 U.S. 167, 180-81 (2000). Allowing plaintiffs to challenge all actions related to mifepristone based on purported injuries from one

action would improperly dispense standing "in gross." *TransUnion*, 141 S. Ct. at 2208.

Nor is that a mere technicality. It is implausible that the incremental effects of the post-2015 changes create new safety concerns such that they will cause an identified plaintiff to treat patients for mifepristone complications. Neither the district court nor the stay panel pointed to any reliable evidence suggesting that those changes have substantially increased adverse events. In fact, adverse events remain extremely infrequent. *See, e.g.*, ROA.829 (discussing FDA's "extensive review of the published literature since March 29, 2016 … through September 30, 2021"); ROA.840 (citing a 2018 study that found "no statistically significant difference between the overall complication rates between an 'at home' and 'at the hospital' abortion"); ROA.2490 (describing "no appreciable difference" in adverse events since FDA's actions in 2016 and thereafter); FDA, *Mifepristone U.S. Post-Marketing Adverse Events Summary through 06/30/2022*, at 1-2, https://perma.cc/LAM4-KVDZ (*Adverse Events Summary*) (reporting adverse events received by FDA through June 30, 2022).

The stay panel suggested that removing the in-person dispensing requirement poses a particular risk to women experiencing undiagnosed ectopic pregnancies. ROA.4392-96 (reasoning that, without a "physical exam to ensure gestational age and/or an ectopic pregnancy," women will be more likely to suffer injury and plaintiffs will be more likely to treat them); *see* ROA.4328. To be clear, mifepristone does not exacerbate ectopic pregnancy; it simply is not effective in treating that condition. As FDA recognized, there are other ways to diagnose ectopic pregnancy, not all of which require an in-person physical exam. ROA.652. The Patient Agreement Form also advises patients to follow up with their providers within two weeks to ensure their pregnancies have ended. *See Mifepristone Patient Agreement Form*, https://perma.cc/FYA4-BQNN; ROA.815 (recommending follow-up pregnancy test).

Plaintiffs' asserted harms related to ectopic pregnancy, like the rest of their alleged injuries, thus rest on a series of speculative events: that a woman with an ectopic pregnancy will be prescribed mifepristone; that her ectopic pregnancy will rupture before she confirms with her provider that she is no longer pregnant; that she will

mistake the debilitating pain associated with an ectopic rupture for the normal medication abortion process; that she will thus delay seeking treatment, contrary to instructions in the Patient Agreement Form, thereby experiencing greater complications than she would have without having taken mifepristone; and that (unidentified) plaintiffs will be forced to treat such complications—despite the fact that ectopic pregnancy occurs in just 0.005% of women who use mifepristone. *See* U.S. Gov't Accountability Office (GAO), GAO-08-751, *FDA: Approval and Oversight of the Drug Mifeprex* 39 (2008), https://perma.cc/JZW3-3J8N (2008 GAO Report) (Stay.Add.418). That theory of standing is foreclosed by Supreme Court precedent and belied by the record. *See supra* pp. 19-26.

2. Plaintiffs Lack Organizational Standing

The district court also erred in concluding that the plaintiff associations have standing based on changes to the adverse event reporting requirements for prescribers under the REMS. ROA.4318-19; *see also* ROA.4399 (reasoning that, in light of those changes, plaintiffs have spent "time, energy, and resources" to "conduct[] their own studies and analyses of available data."). The district court failed to cite any

precedent suggesting that a plaintiff has an Article III injury merely because the government changes reporting requirements applicable only to third parties. More generally, if diversion of resources were sufficient to confer Article III standing, any organization (including the environmental association in *Summers*) would have standing to challenge any government action that it advocates against. But the Supreme Court has made clear that parties who do not face some actual and imminent injury "cannot manufacture standing merely by inflicting harm on themselves." *Clapper*, 568 U.S. at 416.

In any event, even if the district court were correct to find standing based on plaintiffs' alleged informational injury, that would support, at most, an order requiring greater reporting. It would not justify staying any other agency action challenged in this case.[5]

[5] The district court also concluded that lack of information on adverse events undermined plaintiffs' ability to obtain informed consent to prescribe mifepristone. ROA.4314-15. But plaintiffs do not prescribe mifepristone and thus are not required to obtain informed consent from their patients regarding use of mifepristone. Plaintiffs' alleged injury is thus a far cry from the injury alleged in *Havens Realty Corp. v. Coleman*, 455 U.S. 363 (1982), where the plaintiff organization's "purpose" and core "activities" concerned the information at issue. *Id.* at 368; *see id.* at 379-80.

3. Plaintiffs Lack Third-Party Standing

Finally, the district court erred in holding that plaintiffs may assert the interests of women who might take mifepristone in the future, a theory of standing that the stay panel did not adopt. ROA.4315-17. Third-party standing is not a substitute for the "irreducible constitutional minimum of standing," which requires "the plaintiff"—not a third party—to have "suffered an 'injury in fact.'" *Lujan*, 504 U.S. at 560. Instead, third-party standing is an exception to the "prudential" rules that even a plaintiff with injury in fact ordinarily cannot "rest his claim to relief on the legal rights or interests of third parties." *Kowalski v. Tesmer*, 543 U.S. 125, 128-29 (2004).

The Supreme Court has held, for example, that doctors directly regulated by restrictions on abortion may challenge those restrictions by asserting their patients' rights. *See June Med. Servs. L.L.C. v. Russo*, 140 S. Ct. 2103, 2117-20 (2020), *overruled on other grounds*, *Dobbs v. Jackson Women's Health Org.*, 142 S. Ct. 2228 (2022). The district court reasoned that if abortion providers have standing to challenge laws restricting abortion, so too must plaintiffs have standing here. ROA.4316. But this case is entirely different. In *June Medical*,

the doctors' conduct was directly regulated by the challenged restrictions; in contrast, plaintiffs here face no "'threatened imposition of governmental sanctions' for noncompliance" with any agency action related to mifepristone. 140 S. Ct. at 2118-19. Thus, plaintiffs do not merely seek to assert the legal rights of their hypothetical future patients; they seek to use alleged harms to hypothetical third parties to cure their *own* lack of injury. Plaintiffs cite no precedent endorsing such an end-run around Article III's "irreducible constitutional minimum." *Lujan*, 504 U.S. at 560.

Plaintiffs also do not satisfy the requirements for third-party standing. They do not have "a 'close' relationship" with the "as yet unascertained" patients they purport to represent. *Kowalski*, 543 U.S. at 130-31. And they cannot plausibly claim to represent those patients because their interests are diametrically opposed: Plaintiffs seek to block access to mifepristone, but the hypothetical patients they posit are, by definition, women who choose to use the drug after being fully informed about the drug's potential for rare adverse effects. *See Canfield Aviation, Inc. v. NTSB*, 854 F.2d 745, 748 (5th Cir. 1988).

The district court's reasoning about women's interests also finds no support in the record. As discussed, serious adverse events are exceedingly rare. The court posited that women "suffer distress and regret" after using mifepristone, relying on anecdotes from plaintiffs' declarants, its own lay interpretation of two articles, and an amicus brief. ROA.4315-17. But none of those sources provides any basis to overturn FDA's safety judgments. For example, the cited amicus brief relied on a 2021 article based on fewer than 100 anonymous blog posts submitted to a website entitled *Abortion Changes You*. *See* ROA.1514 (conceding that "the population of women who write an anonymous post about their abortion experience may be different from those who do not"). At bottom, the district court's conclusions about women's interests lack merit and ignore the agency of women, who are in the best position to decide what is in their own interests in consultation with their medical providers.[6]

[6] For similar reasons, the district court erred in concluding that plaintiffs who oppose the prescription and use of a drug that FDA has found to be safe and effective are within the zone of interests protected by the FDCA's new drug approval provisions. ROA.4323-24. Plaintiffs' asserted interests are "so marginally related to or inconsistent with" the structure and purposes of the FDCA that they have no basis for suit.

B. Plaintiffs' Central Claims Are Time-Barred

The district court erred by holding that plaintiffs' central claims are timely. *See* ROA.4400-07. Each claim has a six-year statute of limitations. 28 U.S.C. § 2401(a). FDA approved mifepristone in 2000. ROA.591. In 2002, plaintiffs filed a petition challenging certain safety findings and the agency's use of its Subpart H authority, and FDA denied that petition in March 2016. ROA.635-67. Those actions occurred more than six years before plaintiffs filed suit. ROA.185. Plaintiffs' claims challenging the 2000 approval and the 2016 petition denial are thus time-barred.

The district court erred in concluding that FDA reopened those decisions and thereby restarted the statute of limitations. ROA.4325-29. The reopening doctrine does not apply here, where FDA did not undertake "a serious, substantive reconsideration" of its 2000 approval of mifepristone. *See Texas v. Biden*, 20 F.4th 928, 951-52 (5th Cir. 2021), *rev'd on other grounds*, 142 S. Ct. 2528 (2022); ROA.4402-04.

See Match-E-Be-Nash-She-Wish Band of Pottawatomi Indians v. Patchak, 567 U.S. 209, 225 (2012). Similarly, there is no basis to conclude that plaintiffs are within the zone of interests of the Comstock Act, a criminal statute that no private person has a right of action to enforce.

First, FDA did nothing to reconsider its approval of mifepristone when, in 2016, it modified the conditions of use, including the REMS. In 2016, FDA relaxed specific REMS requirements. FDA had already found in 2000 that mifepristone was safe and effective *with* those requirements; the question in 2016 was whether mifepristone would remain safe and effective *without* them. FDA thus evaluated new evidence bearing on whether certain requirements were too restrictive. FDA did not even mention Subpart H, much less reopen its analysis of that issue, which had been rendered irrelevant by FDA's subsequent invocation of the statutory REMS authority. Nor would FDA have needed to revisit these issues in this decision, given that, on the same day, FDA issued a separate decision denying plaintiffs' petition raising these arguments. Plaintiffs did not timely seek review of that decision. They cannot circumvent the statute of limitations by seeking judicial review of a different agency decision predicated on the understanding that mifepristone was properly approved.

Second, FDA did not reopen the approval when it denied plaintiffs' second petition in 2021. An agency does not "trigger the reopen[ing] doctrine" when it denies a petition and "respond[s] to assertions in the

petition." *National Mining Ass'n v. U.S. Dep't of Interior*, 70 F.3d 1345, 1352 (D.C. Cir. 1995). To the contrary, when an agency refuses to rescind a prior decision, judicial review is strictly "limited to the '*narrow issues as defined by the denial of the petition*'" and does not reach "the agency's original action." *NLRB Union v. FLRA*, 834 F.2d 191, 196 (D.C. Cir. 1987). Here, FDA simply responded to plaintiffs' assertions related to the 2016 changes and in-person dispensing. Revoking the underlying approval was not at issue. Indeed, plaintiffs themselves took that approval for granted, affirmatively urging FDA to "restore" the restrictions "approved in 2000" and "retain" the mifepristone REMS. ROA.741.

The district court's reliance on *Sierra Club v. EPA*, 551 F.3d 1019 (D.C. Cir. 2008), was misplaced. *Sierra Club* held that an agency constructively reopened a rule by "significantly alter[ing] the stakes of judicial review" when the original rule "may not have been worth challenging" on its own. *Id.* at 1025-26. As the stay panel recognized, "plaintiffs *did* challenge" mifepristone's original approval on its own (by filing a citizen petition in 2002); they simply failed to timely seek review of FDA's denial of that challenge. ROA.4407. In any event, FDA did

not effect a "sea change" to mifepristone's "basic regulatory scheme" in 2016 or 2021 and thus did not constructively reopen the approval even under the *Sierra Club* framework. *See National Biodiesel Bd. v. EPA*, 843 F.3d 1010, 1017 (D.C. Cir. 2016).

The district court likewise erred in holding that plaintiffs were entitled to equitable tolling, as the stay panel agreed. ROA.4329-31; ROA.4407. Plaintiffs *never even asked* for equitable tolling, because they have no plausible claim to it. Plaintiffs plainly could not establish "'(1) that [they have] been pursuing [their] rights diligently, and (2) that some extraordinary circumstance stood in their way' and prevented timely filing." *Menominee Indian Tribe of Wisconsin v. United States* 577 U.S. 250, 255 (2016).

II. FDA's Challenged Actions With Respect To Mifepristone Were Lawful

Even if plaintiffs' claims were judicially reviewable, they would be unlikely to succeed. FDA's approval of mifepristone and subsequent actions were neither arbitrary and capricious nor contrary to law. "[C]ourts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health." *FDA v. American Coll. of Obstetricians & Gynecologists*, 141 S.

Ct. 578, 579 (2021) (Roberts, C.J., concurring in the grant of application for stay); *see Sierra Club v. EPA*, 939 F.3d 649, 680 (5th Cir. 2019) ("A reviewing court must be 'most deferential' to the agency where, as here, its decision is based upon its evaluation of complex scientific data within its technical expertise.").

The FDCA requires FDA to determine whether a drug is "safe for use" and effective under the proposed conditions of use, 21 U.S.C. § 355(d), such that the drug's "expected therapeutic gain justifies the risk entailed by its use." *United States v. Rutherford*, 442 U.S. 544, 555 (1979). That is what FDA did with respect to mifepristone. *See, e.g.*, ROA.591-98, 637-66 (evidence supporting 2000 approval); ROA.703-24, 809-23, 2147-2241 (2016 changes); ROA.827-38 (in-person dispensing). GAO confirmed that FDA's 2000 and 2016 decisions followed the agency's standard processes. *See* 2008 GAO Report 1 (Stay.Add.377); GAO, GAO-18-292, *FDA: Information on Mifeprex Labeling Changes and Ongoing Monitoring Efforts* 1 (2018), https://perma.cc/Y4WM-8HFZ (Stay.Add.432). The district court's contrary conclusions rest on a series of fundamental errors.

A. FDA Lawfully Approved Mifepristone In 2000

Because the stay panel found plaintiffs' challenge to the 2000 approval likely time-barred, it did not reach the merits of that challenge. In any event, the district court's conclusions with respect to the 2000 approval are incorrect. ROA.4345-64.

1. FDA Reasonably Approved Mifepristone As Safe And Effective Under The FDCA

FDA's 2000 approval of mifepristone plainly was not arbitrary and capricious. FDA "reasonably considered the relevant issues" and "reasonably explained [its] decision." *FCC v. Prometheus Radio Project*, 141 S. Ct. 1150, 1158 (2021). The district court went well beyond its role by concluding otherwise based on its own lay interpretation of the scientific evidence. For example, FDA relied on three clinical trials involving more than 2500 patients demonstrating the drug's safety. ROA.591. Available evidence over the last two decades confirms FDA's determination that mifepristone is safe under the approved conditions of use. More than five million women have used mifepristone to terminate their pregnancies in the United States. *Adverse Events Summary* 1. Mifepristone is also approved in dozens of other countries. ROA.2241 (62 countries as of 2015); Gynuity Health

Projects, *Mifepristone Approved List* (Mar. 2023), https://perma.cc/MHY4-KQNW (94 countries as of 2023). And the World Health Organization has declared it to be an "Essential Medicine." ROA.2154.

Despite such widespread use, serious adverse events have proven "exceedingly rare," as discussed above. ROA.2189; *see supra* pp. 24-26. And even when a patient may need a follow-up surgical procedure, it is often to address incomplete abortions or ongoing pregnancies—not emergency situations. *See supra* p. 25 (distinguishing adverse events from ineffective treatment); ROA.591 (discussing clinical trial in which surgical intervention was provided for 7.9% of patients who used mifepristone, 72% of which were for incomplete abortion or ongoing pregnancies); ROA.642; ROA.839-40. That intervention is better described as an alternative treatment that the patient likely would have pursued in the first instance if mifepristone were unavailable, not as a complication.

The district court questioned FDA's assessment of the data before the agency in 2000, highlighting some subsequent reports of particularly serious events, including deaths. ROA.4359. But the fact

that a drug is associated with an adverse event for reporting purposes does not mean that it actually caused that event. *See supra* p. 26 n.4 (noting that "[n]o causal relationship … has been established"). As of June 2022, only 28 deaths had been reported among the millions of women who have taken mifepristone, and some had obvious alternative causes—including homicide, drug overdose, and other factors entirely unrelated to mifepristone. *See Adverse Events Summary* 1. In addition, pregnancy itself entails a significantly higher risk of serious adverse events, including a death rate 14 times higher than that associated with legal abortion. ROA.638 & n.6. Regardless, the FDCA does not require FDA to approve drugs only when they are without risk—no drug is—but instead to consider whether "the expected therapeutic gain justifies the risk entailed by its use." *Rutherford*, 442 U.S. at 555; *see* 21 U.S.C. § 355(d) (FDA must make a "risk-benefit assessment" that "balance[s] consideration of benefits and risks"). That is what FDA did here.

The district court also criticized FDA for relying on studies with somewhat different protocols than the conditions of use approved by the agency, *e.g.*, ROA.4355, 4365, but this "study match" requirement finds no support in the FDCA. Congress directed FDA to evaluate drug

safety based on "the information submitted … as part of the application" and "any other information" before the agency. 21 U.S.C. § 355(d). No provision requires FDA to limit approval conditions to the precise protocols in clinical trials or existing studies. If Congress had intended such a requirement, it would have imposed one. Instead, Congress granted FDA broad authority to "exercise [its] discretion or subjective judgment in determining whether a study is adequate and well controlled." *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 621 n.17 (1973). Agencies often operate without "perfect empirical or statistical data," and FDA's approval of mifepristone reflected "a reasonable predictive judgment based on the evidence it had." *Prometheus*, 141 S. Ct. at 1160.

Nor is there any scientific basis for a "study match" requirement. As FDA explained, "[m]any clinical trial designs are more restrictive … than will be necessary or recommended in post[-]approval clinical use; this additional level of caution is exercised until the safety and efficacy of the product is demonstrated." ROA.662. FDA thus routinely approves drugs with conditions of use that differ from clinical trial protocols. For example, routine biopsies were performed in trials for

menopause hormonal therapy drugs to establish their safety, but FDA did not require biopsies in those drugs' approved conditions of use. ROA.662; Stay.Add.470-73, 517-18; *see also, e.g.*, Stay.Add.530, 563 (for Aveed, liver function tests required in clinical trials but not approved conditions of use); Stay.Add.599, 632 (for Cialis, same for electrocardiograms); Stay.Add.634, 654 (for Lipitor, same for routine measurement of creatine kinase levels).

Finally, the district court faulted FDA for deferring to medical providers on the appropriate method for dating pregnancies and diagnosing ectopic pregnancies. ROA.4357-65. But FDA merely recognized that health care providers are usually best positioned to make clinical decisions for their patients, and there are a variety of ways to date pregnancies and diagnose ectopic pregnancies. ROA.652; *see supra* pp. 29-30. FDA's reliance on the professional judgment of a patient's healthcare provider is hardly arbitrary and capricious.[7]

[7] The court also mistakenly described FDA as having concluded that mifepristone was *not* safe and effective under the approved conditions. ROA.4356, 4361. That was FDA's evaluation of mifepristone in February 2000 *without* distribution restrictions, ROA.587, but seven months later FDA concluded that "adequate information has been presented to approve" mifepristone *with* those restrictions, ROA.600.

2. FDA Properly Approved Mifepristone Under Subpart H

The district court also erred by holding that FDA's approval of mifepristone in 2000 was invalid under Subpart H of its regulations. ROA.4345-54. The court fundamentally misunderstood FDA's Subpart H authority. Those regulations apply to drugs that treat "serious or life-threatening illnesses" and provide meaningful therapeutic benefits over existing treatments. 21 C.F.R. § 314.500. FDA may restrict a drug's distribution under Subpart H, as it did for mifepristone. *See id.* § 314.520. But the drug *approval* is based on FDA's statutory authority under 21 U.S.C. § 355, not Subpart H. And in 2007, Congress created the new REMS framework and incorporated mifepristone's distribution restrictions into that framework. FDAAA, 121 Stat. 823. FDA has regulated mifepristone under that framework ever since, including by approving a REMS for mifepristone in 2011. ROA.804. The FDAAA and FDA's actions under it supersede and render irrelevant any issues concerning FDA's prior reliance on Subpart H in 2000.

In any event, FDA properly invoked Subpart H. FDA found that pregnancy "can be a serious medical condition in some women," and mifepristone avoided a surgical procedure for 92% of patients.

ROA.598; ROA.637-41; *see also infra* pp. 47-48, 51 (noting even higher efficacy rates reported in more recent trials). The district court reasoned that pregnancy is not an "illness," but the preamble to FDA's final rule explained that Subpart H was available for drugs that treat serious or life-threatening conditions. ROA.638; 57 Fed. Reg. at 58,946-48. Congress ratified this understanding by authorizing FDA to impose similar restrictions under the REMS framework on drugs intended to treat a "disease or condition." 21 U.S.C. § 355-1(a)(1). And while the court disagreed that avoiding a surgical procedure and associated anesthesia is a "meaningful therapeutic benefit," FDA reasonably determined that it is for many patients. ROA.639.

B. FDA Lawfully Changed The Conditions Of Approval In 2016

1. In 2016, FDA approved an application to change mifepristone's conditions of approval by, as relevant here, (a) increasing the gestational age limit from seven to 10 weeks; (b) reducing the number of required clinical visits from three to one; and (c) allowing non-physician health care providers licensed under state law to prescribe and dispense mifepristone. ROA.689-94. The district court erred in holding that these changes were arbitrary and capricious. ROA.4364-66.

FDA based these decisions on an exhaustive review of "data gained in the last 20 years from millions of women in the US and abroad," among other information. ROA.2175; *see* ROA.2160-61 (listing 14 "major studies and review articles covering over 45,000 women"); ROA.2233-40 (listing 79 total publications examining safety and efficacy). And FDA carefully explained how the available scientific evidence supported each change. ROA.703-15. FDA concluded that the evidence relating to the proposed changes "d[id] not suggest a safety profile different from the original approved Mifeprex dosing regimen," ROA.709, which had "exceedingly rare" adverse events, ROA.2189.

To take just a few examples:

- *Increase in gestational age*. FDA examined safety and efficacy data from nearly two dozen studies. ROA.2171-80; ROA.712-13. "Four studies" and a "systematic review" including "over 30,000" women had "evaluated the exact proposed dosing regimen through 70 days gestation." ROA.704. The publications that FDA reviewed showed that mifepristone's success rate at later stages of pregnancy was "comparable to (and in several studies, greater than) the success rates for medical abortion in the initial 2000 decision for Mifeprex up to 49 days gestation." ROA.2180.

- *Reduction in clinical visits*. FDA relied on nearly a dozen studies involving "large numbers of women in the U.S." and other countries, all of which showed that permitting women to complete the two-drug protocol at home was "associated with exceedingly low rates of serious adverse events, and with rates

of common adverse events comparable to those in the studies of clinic administration of misoprostol that supported the initial approval in 2000." ROA.713; *see also* ROA.2182 (citing studies); ROA.2190 (discussing "studies including well over 30,000 patients" that "demonstrat[ed] an acceptable safety profile").

- *Prescriptions by licensed non-physicians*. FDA relied on "four studies with 3,200 women in randomized controlled clinical trials and 596 women in prospective cohorts." ROA.707. Those studies found "no differences in efficacy, serious adverse events, ongoing pregnancy or incomplete abortion" depending on whether a physician provided the drug. ROA.2221. In fact, one study found that mifepristone was *more* effective when provided by nurses instead of physicians. ROA.707.

The district court was wrong to conclude that FDA did not base its decision on studies that reflected the conditions that FDA ultimately adopted. ROA.4365-66; ROA.4411-12. As just shown, the challenged actions were all supported by studies showing that mifepristone is safe and effective when dispensed and used pursuant to the revised conditions.

The stay panel concluded that the 2016 changes were arbitrary and capricious because it did not believe that FDA had cited a study evaluating the effects of those changes "as a whole." ROA.4412. In other words, the panel appeared to hold that FDA cannot change a

drug's conditions of use unless it can cite a single study that combines all of the relevant changes.

As discussed above, however, neither the Administrative Procedure Act nor the FDCA supports such a "study match" requirement. *See supra* pp. 42-44. Here, FDA grounded its judgment in a voluminous body of scientific evidence. ROA.2142-2241; ROA.698-724. The agency carefully explained why the available data supported its conclusion that the 2016 changes would allow the drug to continue to be used safely and effectively—as it has been. ROA.2202-09; ROA.712-15. Neither the district court nor the stay panel suggested that FDA ignored any study in the administrative record. Nor did they identify any evidence that combining the proposed changes would lead to unsafe outcomes. Indeed, neither court's analysis on this point cited the record at all. Instead, both courts effectively required that studies be conducted to produce evidence that would meet a legal requirement that does not exist. But as the Supreme Court explained in rejecting a similar argument, it was not arbitrary and capricious for FDA to "rel[y] on the data it had (and the absence of any countervailing evidence) to

predict" that changes it had determined were safe individually would also be safe collectively. *Prometheus*, 141 S. Ct. at 1159.

In any event, numerous studies FDA examined combined aspects of the challenged modifications, such that FDA relied on data from those studies "to support multiple changes." ROA.703. And FDA considered at least two studies that closely mirrored the 2016 conditions. Sanhueza Smith et al. 2015 (cited at ROA.704 n.3) considered the relevant dosing regimen through 70 days of gestation. Similarly, Winikoff et al. 2012 (cited at ROA.704 n.1) was also consistent with the 2016 changes, except the authors required study participants to have a gestational age of 57 through 70 days confirmed using ultrasound. The studies FDA reviewed thus strongly supported the agency's conclusion that the combined modifications would not change mifepristone's well-established safety or effectiveness profile.

2. FDA also changed other conditions of use that plaintiffs have not challenged, such as the approved dosing regimen. For example, in 2016, FDA reduced the amount of mifepristone in the dosing regimen from 600 mg to 200 mg, a threefold *reduction*. ROA.2148. FDA also increased the amount of misoprostol, reduced the amount of time

between taking mifepristone and misoprostol, and changed the route of administration of the misoprostol from oral to buccal. ROA.2148. FDA made these changes based on "evidence from the published medical literature" demonstrating their safety and effectiveness. ROA.2148; *e.g.*, ROA.2170-73 (citing "15 studies using the proposed doses (200 mg [of mifepristone] plus 800 mcg [of misoprostol]) with a 24-48 hour dosing interval"); ROA.2164 ("Data from the original US trial … showed lower efficacy rates with the originally approved Mifeprex dosing than is reported in a large number of subsequent trials using different mifepristone-misoprostol dosing regimens," without "any change in the safety profile.").

Plaintiffs have not specifically challenged those changes in this litigation, and neither the district court nor this Court during stay proceedings suggested they were unlawful. Consequently, if this Court determines that any of FDA's 2016 actions were unlawful, it should clarify that its decision extends only to the changes specifically challenged by plaintiffs in their preliminary injunction motion and does not require FDA to revert to an outdated dosing regimen.

C. FDA Lawfully Changed The Adverse Event Reporting Requirements In 2016

In 2016, FDA also changed the requirement that prescribers of mifepristone agree to report certain adverse events, such as hospitalizations and blood transfusions, to the drug's sponsor—a requirement that applied above and beyond FDA's standard reporting requirements for all sponsors of approved drugs. ROA.724; ROA.822. The district court erred in holding that this change was arbitrary and capricious.

The district court criticized FDA's decision on the ground that it "systematically ensur[ed] that almost all new adverse events would go unreported or underreported." ROA.4365. But the court made no effort to address FDA's eminently reasonable explanation for this change. FDA determined that "after 15 years of reporting serious adverse events, the safety profile for Mifeprex is essentially unchanged." ROA.724. By 2016, mifepristone's "well-characterized safety profile" was firmly established, and continued reporting of non-fatal adverse events by prescribers under the REMS was "not warranted" because mifepristone's "known risks occur[] rarely." ROA.822.

Moreover, FDA did not eliminate all adverse event reporting requirements. FDA still requires certified prescribers to report any deaths to the sponsors, and prescribers and patients can voluntarily report other adverse events. And, as with all approved prescription drugs, FDA requires mifepristone's sponsors to report all "serious and unexpected" adverse events to FDA within 15 days and to report all other adverse events annually. *See* ROA.822; 21 C.F.R. §§ 314.80, 314.98. Sponsors also are required to develop procedures for the surveillance, evaluation, and reporting of adverse drug experiences to FDA. 21 C.F.R. § 314.80(b). Nor are reports to FDA the only way to know about adverse events associated with a drug. FDA's regulation of mifepristone has drawn on extensive scientific literature, not just FDA's adverse event database. *See, e.g.*, ROA.829-30.

D. FDA Lawfully Approved Generic Mifepristone In 2019

The district court halted FDA's approval of generic mifepristone solely based on its conclusion that the approval of branded mifepristone was unlawful. ROA.4366; *see* 21 U.S.C. § 355(j)(2). Consequently, if FDA's approval of Mifeprex stands as it should (whether because

plaintiffs' challenge to that approval is time-barred or otherwise fails), FDA's approval of generic mifepristone must stand as well.

E. FDA Lawfully Determined That The In-Person Dispensing Requirement Should Be Removed

The district court likewise erred in concluding that FDA unlawfully removed the in-person dispensing requirement for mifepristone. ROA.4338-45.

1. FDA's decision to remove the in-person dispensing requirement was not arbitrary and capricious. The agency decided in 2021 to lift the in-person dispensing requirement because the evidence showed that such a requirement was no longer needed to assure mifepristone's safe use. ROA.829-38. FDA's decision "was the result of a thorough scientific review by experts within FDA's Center for Drug Evaluation and Research (CDER), who evaluated relevant information, including available clinical outcomes data and adverse event reports." ROA.807.

The district court, like the stay panel, concluded that FDA unreasonably removed the in-person dispensing requirement, suggesting that the agency's decision was based on an artificial lack of data caused by FDA's decision "to practically eliminate an 'adverse event' reporting requirement." ROA.4344-45; ROA.4412. This

assertion misunderstands the record. As explained above, when FDA changed the reporting requirements under the REMS for certified prescribers to report certain adverse events to the sponsor, it left undisturbed the detailed reporting requirements governing mifepristone's sponsors. *See supra* pp. 52-53. And, as FDA explained, adverse event reports are contained in the FDA Adverse Event Reporting System database, which FDA "routinely monitors." ROA.828. FDA's decision to remove the in-person dispensing requirement fully considered information about all adverse event reports it had received. ROA.828-29.

Moreover, adverse event reports were not the only evidence FDA considered in 2021. FDA also specifically reviewed data from the drug's sponsors and other sources and concluded that nonenforcement of the in-person dispensing requirement during periods in 2020 and 2021 did not appear to affect adverse events. ROA.827-29. FDA further relied on "an extensive review of the published literature," including studies that "examined replacing in-person dispensing in certain healthcare settings with dispensing at retail pharmacies" and "dispensing mifepristone from pharmacies by mail." ROA.829-30. FDA's analysis of

those studies spans nearly 10 full pages in the 2021 petition response. ROA.829-38; *see also* FDA, *REMS Modification Rationale Review* 19-42 (2021), https://perma.cc/W4U3-L38P (analyzing REMS assessment reports, numerous published studies involving thousands of patients, and other data to conclude that "mifepristone will remain safe and effective for medical abortion if the in-person dispensing requirement is removed"). But neither the district court nor the stay panel acknowledged FDA's analysis or explained why it was insufficient.

2. The district court also concluded that removing the in-person dispensing requirement was contrary to law based on statutory provisions derived from the 1873 Comstock Act. ROA.4338-44. In their current form, those provisions restrict the importation, mailing, or interstate distribution by common carrier of (among other items) drugs "intended for producing abortion." 18 U.S.C. §§ 1461, 1462. The court's reliance on the Comstock Act was doubly flawed: The Comstock Act is not relevant to FDA's exercise of its authority under the FDCA, and the court misinterpreted the Comstock Act.

a. The FDCA requires FDA to assess safety and effectiveness when it approves a drug and sets the conditions for its use. *See* 21

U.S.C. §§ 355(d), 355-1. Nothing in the statute requires FDA to address in those decisions other laws that may restrict the drug's distribution or use. Instead, the FDCA properly leaves enforcement of those laws to the agencies charged with their administration. For example, the Controlled Substances Act restricts distribution of fentanyl, but FDA has not incorporated those restrictions into its approval or REMS for certain fentanyl products. *Transmucosal Immediate Release Fentanyl Shared System REMS Program* (Dec. 2022), https://perma.cc/JK6T-S99C; 21 U.S.C. §§ 841-843.

b. Regardless, the district court misinterpreted the Comstock Act. As originally enacted, the Comstock Act prohibited selling drugs for "causing unlawful abortion" (among other items) in federal territories, Act of Mar. 3, 1873, ch. 258, § 1, 17 Stat. 598, 598-99; mailing drugs for "procuring of abortion," *id.* § 2, 17 Stat. at 599; and importing the "hereinbefore-mentioned articles," *id.* § 3, 17 Stat. at 599. The next year, Congress clarified that the importation restriction, like the federal territory restriction, was limited to drugs for "causing *unlawful* abortion." Rev. Stat. § 2491 (1st ed. 1875), 18 Stat. pt. 1, at 460 (emphasis added). Despite "slight distinctions in expression," the Act's

restrictions were part of a unified scheme, and courts and the Postal Service interpreted all of the restrictions as limited to articles to be used unlawfully. *See, e.g.*, *United States v. One Package*, 86 F.2d 737, 739 (2d Cir. 1936); *id.* at 740 (Learned Hand, J., concurring); *Application of the Comstock Act to the Mailing of Prescription Drugs That Can Be Used for Abortions*, 46 Op. O.L.C. __, at 5-11 (Dec. 23, 2022) (OLC Op.) (Stay.Add.262-68). Congress ratified that established construction by repeatedly amending the Comstock Act without material change *after* that construction had been called to the "attention of Congress" in a Historical and Revision Note set out in the United States Code itself since 1948. *See* OLC Op. 12-15 (Stay.Add.269-72); 18 U.S.C. § 1461 note.

Moreover, by 1965, FDA had approved at least seven oral contraceptives, even though contraceptives were still among the Act's enumerated items. *See* Lara Marks, *Sexual Chemistry: A History of the Contraceptive Pill* 77-78 (2001). Congress repeatedly amended the FDCA without limiting FDA's authority to approve types of drugs enumerated in the Comstock Act. *See, e.g.*, Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780.

The district court ignored this history, emphasizing what it regarded as the Act's "plain text." ROA.4340-41. But reading the words in their context and with a view to their place in the overall statutory scheme, the Act never prohibited the distribution of abortion drugs for lawful uses. *See FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000). At most, the texts of the various provisions are internally inconsistent: The statute does not uniformly specify whether it applies to drugs for "any" or only "unlawful" abortion. 18 U.S.C. §§ 1461, 1462. Various versions of the statute used "abortion" and "unlawful abortion" interchangeably (and one, 19 U.S.C. § 1305(a), still includes the adjective). Neither the district court nor the stay panel cited even a single prior decision holding that the Comstock Act prohibits the mailing of drugs for lawful purposes.

Thus, at a minimum, the Act does not speak "clearly" enough to have "significantly changed the federal-state balance" by applying to drugs used lawfully. *See United States v. Bass*, 404 U.S. 336, 349 (1971). Making it a federal crime to mail drugs for lawful medical purposes would significantly upset the federal-state balance by interfering with state "health and welfare laws." *See Dobbs*, 142 S. Ct.

at 2284; 18 U.S.C. § 1461 note ("The intention to prevent a proper medical use of drugs or other articles merely because they are capable of illegal uses is not lightly to be ascribed to Congress." (quoting *Youngs Rubber Corp. v. C.I. Lee & Co.*, 45 F.2d 103, 108 (2d Cir. 1930))).

In any event, when Congress enacted the FDAAA in 2007, Congress "deemed" drugs like mifepristone to have an enforceable REMS containing "any" existing conditions. FDAAA § 909(b), 121 Stat. at 950-51; ROA.641. And Congress was well aware that it was authorizing mifepristone's distribution system to continue. *See* ROA.315 (staff report prepared for Congressman Souder following 2006 subcommittee hearing on mifepristone); 153 Cong. Rec. S5765 (daily ed. May 9, 2007) (statement of Sen. Coburn recognizing that mifepristone "is deemed to have a REMS and is subject to periodic review"); 153 Cong. Rec. S5469 (daily ed. May 2, 2007) (similar statement of Sen. DeMint). One failed Senate proposal would have treated mifepristone differently from other Subpart H drugs. *See* S. 1082, 110th Cong. § 214(b)(3)(B) (2007). Another would have suspended mifepristone's approval entirely. Inside Washington's FDA Week, *GOP Fails to Narrow Scope of FDA Reform Bill During Senate Mark-Up*, vol. 13,

no. 16, at 1, 13-14 (Apr. 20, 2007). Congress chose, however, to treat mifepristone the same as other Subpart H drugs.

The FDAAA thereby superseded any application of the Comstock Act to mifepristone. Since mifepristone's approval in 2000, the drug has been imported and distributed interstate, as FDA's approval allowed (and as Congress knew). *See* ROA.315; *e.g.*, ROA.596 (requiring "[s]ecure shipping procedures"). The "plain import" of Congress's decision to provide for mifepristone's existing distribution system to continue is that the Comstock Act does not bar those same activities. *See Dorsey v. United States*, 567 U.S. 260, 274-75 (2012).

3. Relatedly, the district court erroneously held that FDA's exercise of enforcement discretion with respect to in-person dispensing during the COVID-19 public health emergency was judicially reviewable, ROA.4331-33, and unlawful, ROA.4338-45. That claim became moot when FDA revised the REMS in January 2023 to remove the in-person dispensing requirement. *See supra* p. 11. In any event, vacatur of the district court's order would be warranted because the COVID-19 public health emergency ends on May 11, 2023, at which point FDA's enforcement discretion policy would expire regardless.

See DeOtte v. State, 20 F.4th 1055, 1064 (5th Cir. 2021) (citing *United States v. Munsingwear, Inc.*, 340 U.S. 36, 39 (1950)).

III. The District Court Abused Its Discretion In Awarding Preliminary Relief

The district court's abrupt and sweeping "stay" of multiple agency actions, some more than 20 years old, is contrary to established equitable principles.

1. As an initial matter, the district court erred in the form of relief it ordered. Although the plaintiffs sought a preliminary injunction requiring FDA to withdraw or suspend the approval of mifepristone, the district court sua sponte invoked 5 U.S.C. § 705—which authorizes a court in an APA action "to postpone the effective date of an agency action or to preserve status or rights pending conclusion of review proceedings"—to "stay" the effective date of FDA's 2000 approval of mifepristone and all subsequent actions.

That was error. Plaintiffs failed to seek a stay of the relevant actions pending judicial review from FDA itself, as required by regulation. 21 C.F.R. § 10.45(c). Moreover, the relevant statutory authorization to "postpone" the effective date of a challenged action indicates that the stay must be contemporaneous with the challenged

action, not years or decades later. And, in any event, the statutory text makes clear that § 705 relief is intended to preserve the status quo pending judicial review, not, as here, dramatically upend it. *See also* H.R. Rep. No. 1950, 79th Cong., 2d Sess. (1946).

2. The purpose of any preliminary relief, moreover, "is to preserve the status quo and thus prevent irreparable harm" before the merits are decided. *See City of Dallas v. Delta Air Lines, Inc.*, 847 F.3d 279, 285 (5th Cir. 2017). The district court upended the status quo with an abrupt and sweeping nationwide order that will profoundly harm women, the Nation's healthcare system, FDA, the sponsors, and the public interest generally.

Congress empowered FDA to ensure that drugs are safe and effective. FDA has done so with respect to mifepristone. The district court's order arrogates that authority to the detriment of women across the country. For many patients, mifepristone is the best method to lawfully terminate their pregnancies. They may choose mifepristone over surgical abortion for reasons such as medical necessity or past trauma. ROA.2468-70; ROA.2478-85; ROA.2510-11. Surgical abortion is an invasive medical procedure that may have greater health risks for

some patients, such as those who are allergic to anesthesia. ROA.596-98; ROA.639; ROA.2466-67; ROA.2478, 2481; ROA.2501; ROA.2509-10. Surgical abortion is also often unavailable for practical reasons even when abortion is lawful, and travel costs could place abortion entirely out of reach for some patients. ROA.2482-85 (explaining that one of 18 Maine Family Planning clinics offers surgical abortion). Deprivation of "necessary medical care" imposes irreparable harm. *Jones v. Texas Dep't of Criminal Justice*, 880 F.3d 756, 759-60 (5th Cir. 2018) (per curiam).

Those harms would be felt throughout the country. Many States broadly permit first-trimester abortions. Even in States with more restrictive laws, abortion is lawful under circumstances where mifepristone may be the best treatment option. *See, e.g.*, Tex. Health & Safety Code Ann. § 170A.002(b) (certain health risks); Miss. Code Ann. §§ 41-41-34.1, 41-41-45(2) (rape); *see also* OLC Op. 17-20 (Stay.Add.274-77). The government also understands that mifepristone is used for non-abortion purposes, including miscarriage management, a reality that underscores the larger potential effects of the court's order. For example, while Wyoming recently passed a law to prohibit

mifepristone's use in many circumstances, it sought to preserve access to mifepristone for miscarriage management. SF0109, § 1(b)(ii), 67th Leg., 2023 Gen. Sess. (Wyo. 2023). If given nationwide effect, the order thus would foreclose or make it more difficult for residents in all States to access a treatment option that may best serve their needs.

Limiting access to mifepristone would further harm patients by unnecessarily burdening the healthcare system. Patients limited to surgical abortions would face long waits for care from a limited number of providers capable of providing the procedure, causing harms to them, their families, and providers. ROA.2440-49. Other patients would experience related harms, as they too wait for healthcare in a system with limited providers and resources being unnecessarily diverted to surgical abortions. ROA.2440-49.

Furthermore, as more than 400 members of the biopharmaceutical industry have warned, the court's order puts "an entire industry focused on medical innovation at risk." *In Support of FDA's Authority to Regulate Medicines*, https://perma.cc/FML8-V2QM. By setting "a precedent for diminishing FDA's authority over drug approvals," the order "creates uncertainty for the entire biopharma industry." *Id.* "If

courts can overturn drug approvals without regard for science or evidence, or for the complexity required to fully vet the safety and efficacy of new drugs, any medicine is at risk for the same outcome as mifepristone." *Id.*

The stay panel suggested that the district court's order would not harm *FDA*, but the interests of the government and the public "merge" in this context. *Nken v. Holder*, 556 U.S. 418, 435 (2009). And "[a]ny time a State is enjoined by a court from effectuating statutes enacted by representatives of its people, it suffers a form of irreparable injury." *Maryland v. King*, 567 U.S. 1301, 1303 (2012) (Roberts, C.J., in chambers). A fortiori that is true for the federal government, which is responsible for implementing Acts of Congress that serve and protect the people of all States. FDA is irreparably harmed when it is blocked from fulfilling its statutory responsibilities consistent with its scientific judgment.

FDA is also irreparably harmed by the disruptive practical effects of the court's order, even if upheld only in part. Attempting to adjust the regulatory scheme during the pendency of further litigation in the district court would impose substantial costs that would be incurred

again if the court's conclusions are ultimately reversed on the merits. *See* Declaration of Janet Woodcock, M.D., Stay Application at 115a-116a, *U.S. FDA v. Alliance for Hippocratic Med.*, No. 22A902 (U.S. Apr. 14, 2023), https://perma.cc/SKB8-4Q7U.

3. In contrast, plaintiffs' alleged harms are attenuated and speculative. They do not remotely justify upending the status quo.

The district court concluded that plaintiffs would be irreparably harmed if called upon to treat patients experiencing serious adverse events after taking mifepristone. ROA.4367. As discussed above, however, serious adverse events are "exceedingly rare," ROA.2189, and plaintiffs have not shown that any identified member will imminently be called upon to treat a woman experiencing such an event. Rather, plaintiffs' claims of irreparable harm—like their standing allegations—rely on speculation that hypothetical patients suffering rare adverse events will seek plaintiffs' care. Yet plaintiffs' own experiences confirm mifepristone's safety profile: Despite mifepristone's widespread use for decades, plaintiffs describe only a handful of times they or their members ever treated a patient for alleged complications from mifepristone. *See supra* p. 21. It is wholly implausible that their

practices would be materially affected by such cases during the pendency of this litigation, particularly for plaintiffs in States where abortion is largely banned.

In addition, plaintiffs' litigation choices demonstrate the lack of equity in immediately blocking lawful distribution of an FDA-approved drug that has been used by millions of patients over two decades. In 2016, FDA denied plaintiffs' petition challenging the drug approval, and plaintiffs waited more than six years to seek judicial review. After FDA approved the 2016 changes, plaintiffs waited more than three years even to file a citizen petition challenging those changes and did not file this suit until nearly a year after that petition was denied. Their "unnecessary, years-long delay in asking for preliminary injunctive relief weigh[s] against their request." *Benisek v. Lamone*, 138 S. Ct. 1942, 1944 (2018) (per curiam). Plaintiffs also encouraged the district court to consolidate their preliminary injunction motion with a bench trial, demonstrating that their interests would not be prejudiced by forgoing preliminary relief and waiting months for trial. *See* ROA.3250. Plaintiffs' own conduct thus confirms that there is no basis—in either irreparable harm or the broader equities—for extraordinary nationwide

relief that would inflict grave harm on women, the medical system, FDA, the sponsors, and the public generally.

CONCLUSION

The district court's order should be reversed.

Respectfully submitted,

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APRIL 2023

CERTIFICATE OF SERVICE

I hereby certify that, on April 26, 2023, I electronically filed the foregoing brief with the Clerk of the Court by using the appellate CM/ECF system. I further certify that the participants in the case are CM/ECF users and that service will be accomplished by using the appellate CM/ECF system.

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limit of Federal Rule of Appellate Procedure 32(a)(7)(B) because it contains 12,687 words according to the count of Microsoft Word. This brief also complies with the typeface and type-style requirements of Federal Rule of Appellate Procedure 32(a)(5) and (6) because it was prepared in Century Schoolbook 14-point font, a proportionally spaced typeface.

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