No. 22A___

IN THE

Supreme Court of the United States

DANCO LABORATORIES, L.L.C.,

Applicant,

v.

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.,

Respondents.

EMERGENCY APPLICATION FOR STAY OF PRELIMINARY INJUNCTION PENDING APPEAL

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RULE 29.6 STATEMENT

Danco Laboratories, LLC is 100% owned by Danco Investors Group, LP.

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**TO THE HONORABLE SAMUEL A. ALITO, JR.,
ASSOCIATE JUSTICE OF THE SUPREME COURT AND
CIRCUIT JUSTICE FOR THE FIFTH CIRCUIT:**

INTRODUCTION

The Fifth Circuit's unprecedented order has created regulatory chaos across the country. The direct consequence of the Fifth Circuit's ruling is that FDA must effectuate a series of extensive approvals to implement the Fifth Circuit's rollback. Without those approvals, Danco cannot legally market and distribute mifepristone. But FDA is simultaneously under court order from the Eastern District of Washington enjoining it from changing any aspect of its regulation and approval of mifepristone in the 17 States plus the District of Columbia that are plaintiffs to that suit. The result is an untenable limbo, for Danco, for providers, for women, and for health care systems all trying to navigate these uncharted waters—and all after Plaintiffs waited years and years before claiming irreparable injury and a need for an emergency injunction voiding the decades-long status quo.

The panel's decision equally upends previously settled standing precedent. This Court's settled view is that neither statistical evidence nor chains of discretionary actions by independent third-parties equates to the certain, impending injury required for Article III standing. That is no less true here than in the many cases where this Court has laid down these rule-of-law principles. The Fifth Circuit's standing analysis flunks those precedents. Worse yet, the panel never even purported to analyze how even those statistics and third-party chains of conduct link to any injury caused by the specific agency actions the panel left enjoined—FDA's 2016 REMS

modifications and subsequent challenged actions. But courts are required to ensure plaintiffs have standing for each claim they press. Absent facts demonstrating certain, impending injury *from those specific FDA actions*, distinct from facts about injury related to their separate challenge to the 2000 approval, there was no basis for the Fifth Circuit to conclude Plaintiffs likely have standing to challenge the 2016 REMS modification and its subsequent actions.

The Fifth Circuit's ruling is equally flawed on the merits. Rather than defer to FDA's expertise in evaluating data from dozens of clinical trials, which members of this Court have repeatedly said courts should do,[1] the Fifth Circuit held that FDA fails to examine " 'an important aspect of the problem' " by making a change to a drug's approval where "zero studies" incorporated all of the exact metes and bounds of the modified approval. App. 35a (citation omitted). The pharmaceutical industry could not have been clearer that such a judicial imposition on FDA of this sort of rigid matching requirement, untethered to anything in the statute or regulations, would be devastating. If that were the rule governing FDA approvals, it would be unlikely that *any* drug on the market is properly approved. Pharmaceutical Companies' Amicus Br., 5th Cir. ECF No. 118 at 34. The Fifth Circuit not only endorsed the District

[1] *See, e.g.*, *Food & Drug Admin.* v. *Am. Coll. of Obstetricians & Gynecologists,* 141 S. Ct. 578, 578-579 (2021) (Roberts, C.J., concurring in grant of application for stay) ("[C]ourts owe significant deference to the politically accountable entities with the 'background, competence, and expertise to assess public health.'"); *Cytori Therapeutics, Inc.* v. *Food & Drug Admin*., 715 F.3d 922, 927 (D.C. Cir. 2013) (Kavanaugh, J.) ("A court is ill-equipped to second-guess that kind of agency scientific judgment under the guise of the APA's arbitrary and capricious standard."); *Otsuka Pharm. Co.* v. *Burwell*, 302 F. Supp. 3d 375, 403 (D.D.C. 2016) (Jackson, J.) ("To begin with, the FDA is an expert agency charged with making precisely these sorts of highly technical determinations, and its interpretation of romanette iv is premised on ' the agency's evaluations of scientific data within its area of expertise.'"), *aff'd sub nom. Otsuka Pharm. Co.* v. *Price*, 869 F.3d 987 (D.C. Cir. 2017).

Court's flawed reasoning—it doubled down, affirming the District Court's blatant second-guessing of FDA's determinations by engaging in that same conduct itself. As nearly 700 members of the biomedical industry; a dozen physicians' groups and health societies; former FDA and DOJ officials; and numerous states, local governments, and members of Congress have recognized, these paradigm-shifting holdings inject confusion, uncertainty, and expense into the regulation of an industry that plays a foundational role in the health and safety of millions of Americans.

Leaving the Fifth Circuit's ruling in place will irreparably harm Danco, which will be unable to both conduct its business nationwide and comply with its legal obligations under the FDCA nationwide. The lack of emergency relief from this Court will also harm women, the healthcare system, the pharmaceutical industry, States' sovereignty interests, and the separation-of-powers.

The Court should stay the District Court's preliminary injunction in full pending appeal. In the alternative, the Court should grant certiorari before judgment and set this case for expedited briefing and argument before the summer recess.

STATEMENT

A. Factual Background

Danco holds the approved New Drug Application (NDA) for Mifeprex (mifepristone) Tablets, a drug approved by FDA for use in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. Mifeprex is Danco's only product.

Following a lengthy approval process where FDA reviewed extensive data demonstrating Mifeprex's safety and efficacy, and consistent with the recommendation from its outside expert advisors, FDA approved the Mifeprex NDA in 2000 for the medical termination of intrauterine pregnancy through 49 days' pregnancy ("2000 approval" or "2000 NDA"). FDA's approval of the Mifeprex NDA was based on its authority in 21 U.S.C § 355 to approve NDAs, and it imposed distribution on use based on its authority in 21 C.F.R. Part 314 Subpart H (Subpart H).

In 2002, some Plaintiffs petitioned FDA to revoke Mifeprex's approval ("2002 petition"). D. Ct. ECF No. 1-14.[2] FDA denied that petition in 2016 in a response that meticulously reviewed the meaningful therapeutic benefit that medical abortion provides over surgical abortion, and thoroughly explained why Mifeprex was safe and effective.

In 2008, Danco submitted a risk evaluation and mitigation strategy (REMS) pursuant to 21 U.S.C. § 355-1(a)(1), which FDA approved in June 2011 ("2011 REMS"). D. Ct. ECF No. 1-30 at 2. The approved REMS maintained the Subpart H requirements imposed with the initial approval of Mifeprex. D. Ct. ECF No. 1-31. Mifepristone's approval has been pursuant to the approved REMS since then.

In 2016, after Danco submitted a supplemental new drug application (sNDA) submitted by extensive data from dozens of clinical studies to support its proposed changes, FDA approved changes to Mifeprex's indication and dosing regimen after

[2] Unless otherwise specified, references to "D. Ct. ECF" are to the District Court docket, No. 2:22-cv-00223-Z (N.D. Tex.), and references to "5th Cir. ECF" are to the Fifth Circuit docket, No. 21-10362 (5th Cir.). All ECF page numbers reference the blue ECF headers.

analyzing the data and determining that data demonstrated Mifeprex continued to be safe and effective under the revised conditions ("2016 changes"). D. Ct. ECF No. 1-32 at 2; D. Ct. ECF No. 1-33 at 7-19. That data included more than 20 studies of the proposed new doses with a 24-48 hour dosing interval. D. Ct. ECF 28-1 at 33-37. The proposed new doses decreased the amount of mifepristone from 600 mg to 200 mg. FDA summarized the studies with one table for the 16,794 subjects in the U.S. studies and another table of the 18,425 subjects in the non-U.S. studies as follows:

Clinical Review
(b) (6) and (b) (6)
NDA 020687/S-020- Mifeprex

Table 3: Efficacy- Mifepristone 200 mg with Buccal Misoprostol 800 mcg 24-48 Hours Later - US Studies

Study &Year	Design, Location	Gestation (maximum days)	M-M Interval (hrs)	Evaluable Subjects (N)	Success - no intervention (%)
Middleton 2005[24] US	Prospective	56	24-48	216	94.9
Winikoff 2008[23] US	Prospective	63	24-36	421	96.2
Fjerstad 2009[27] US	Retrospective	59	24-48	1,349	98.3
Grossman 2011[36] US - Clinic Mife v. Tele-med	Prospective	63	24-48	449	Clinic: 96.9% Telemed: 98.7%
Winikoff 2012[19] US	Prospective	57-70	24-48	629	93.2
Gatter 2015[13] US	Retrospective	63	24-48	13,373	97.7
Chong 2015[17] US	Prospective	63	24-48	357	96.7
TOTALS	**7 Studies**	**56-70 days**	**24-48 hr**	**16,794**	**97.4**

Source: Modified from Table 3, page 14-15, Chen-Creinin 2015 Review and submitted articles. All subjects had 200 mg oral mifepristone followed by 800 mcg buccal misoprostol.
Success percentages calculated by clinical reviewer.

D. Ct. ECF No. 28-1 at 34.

Table 4: Efficacy- Mifepristone 200 mg with Buccal Misoprostol 800 mcg 24-48 Hours Later- Non- US Studies

Study &Year/Country	Design, Location	Gestation (maximum)	M-M Interval (hrs)	Evaluable Subjects (N)	Success - no intervention (%)
Alam 2013[37] Bangladesh	Prospective	63	24	629	92.7
Blum 2012[70]	Prospective	63	24	210	92.9
Boersma 2011[22] Curacao	Prospective	70	24-48	307	97.7
Chai 2013[38] Hong Kong	Prospective	63	48	45	95.6
Dahiya 2012[39] India	Prospective	50	24	50	92
Chong 2012[40] Georgia, Vietnam	Prospective	63	36-48	560	96.4
Giri 2011[41] Nepal	Prospective	63	24	95	93.6
Goldstone 2012[20] Australia	Retrospective	63	24-48	11,155	96.5
Louie 2014[14] Azerbaijan	Prospective	63	24-48	863	97.3
Ngo 2012[42] China	Retrospective	63	36-48	167	91.0
Ngoc 2011[43] Vietnam	Prospective	63	24	201	96.5
Ngoc 2014[16] Vietnam	Prospective	63	24-48	1,371	94.7
Olavarietta 2015[85] Mexico	Prospective	70	24	884	98.2
Pena 2014[44] Mexico	Prospective	70	24-48	971	97.3
Sanhueza 2015[48] Mexico	Prospective	70	24-48	896	93.3
TOTALS	15 Studies	56-70 days	24-48 hrs	18,425	96.1%

Source: Modified from Table 3, page 14-15, Chen-Creinin 2015 Review and submitted articles. All subjects had 200 mg oral mifepristone followed by 800 mcg buccal misoprostol.

Success percentages calculated by clinical reviewer.

D. Ct. ECF No. 28-1 at 35-36.

The FDA reviewer's comment summarizes the data in this way:

> The data above in Table 3 and Table 4 from ~16,800 US women and ~18,400 non-US women in clinical studies of MAB through 70 days gestation with success rates of 97.4% (US) and 96.1% (non-US) strongly support the proposed new dosing regimen and the extension of the acceptable gestational age. The number of US and non-US studies, the number of evaluable women, and the overall complete abortion rates (termination with no surgical intervention) will be described in the efficacy table in Section 14 CLINICAL STUDIES in the new approved label.

D. Ct. ECF No. 28-1 at 36.

FDA carefully analyzed the literature for information about adverse events, describing studies reporting that "29 women of 13,221 (0.1%) undergoing medical abortion experienced a major complication, which was defined as including: emergency department presentation, hospitalization, infection, perforation and hemorrhage requiring transfusion," a study of medical abortion provided through telemedicine that found "[f]our of 1,172 telemedicine patients (0.3%) required a blood transfusion compared to 0.1% of 2,384 in-person patients," and a study that "provides data on other serious adverse events through 70 days." D. Ct. ECF No. 28-1 at 61. The FDA reviewer concluded:

> Serious adverse events including death, hospitalization, serious infection, bleeding requiring transfusion and ectopic pregnancy with the proposed regimen are rarely reported in the literature. The rates, when noted are exceedingly rare, with rates generally far below 1.0% for any individual adverse event. This indicates that medical abortion with the proposed regimen up through 63 days is safe.
>
> Serious fatal or nonfatal adverse events in the 64-70 days gestation group, were evaluated in one US study (Winikoff 2012). This study with 379 women in the 64-70 day range is reassuring in that the rates of hospitalization, serious infection and transfusion are no higher than in the lower gestational age ranges. Based on the available safety data on medical abortion in totality, it appears that serious fatal or nonfatal adverse

> events are very rare through 70 days as well. This regimen should be approved for use through 70 days gestation.

D. Ct. ECF No. 28-1 at 61-62 (internal footnote omitted).

FDA's Clinical Review also involved "a comprehensive review of the adverse events associated with Mifeprex from September 28, 2000 through November 17, 2015." D. Ct. ECF No. 28-1 at 2151. It included a table showing the numbers of "any adverse event," "hospitalization[s], excluding deaths," "transfusions," and "severe infections" from the more than 2.5 million women who had taken mifepristone at that time. D. Ct. ECF No. 28-1 at 2152. The table of adverse events showed that fewer than one-tenth of one percent of women experienced any adverse event, and that far fewer than that already tiny number of women experienced the other listed adverse events. The table summarizing FDA's findings of adverse events from both reporting systems in place during these 15 years is here:

Table 21: US Postmarketing AEs- Mifepristone for Medical Abortion

Date ranges of reports received	09/28/00[†]-10/31/12	11/1/12 - 04/30/14[‡]
Cases with any adverse event	2740	504
Hospitalized, excluding deaths	768	110
*Experienced blood loss requiring transfusions[§]	416	66
Infections[‖] (*Severe infections[¶])	308 (57)	37 (5)

† U.S. approval date.
‡ FDA implemented FAERS on September 10, 2012, and migrated all of the data from the previous reporting system (AERS) to FAERS. Differences may exist when comparing case counts in AERS and FAERS. FDA validated and recoded product information as the AERS reports were migrated to FAERS. As a result of this change, it is not recommended to calculate a cumulative number when reviewing the data provided in Table 5.
* The majority of these women are included in the hospitalized category in Table 5.
§ As stated in the approved Mifeprex (mifepristone) labeling, bleeding or spotting can be expected for an average of 9-16 days, and may last for up to 30 days. Excessive vaginal bleeding usually requires treatment by uterotonics, vasoconstrictor drugs, curettage, administration of saline infusions, and/or blood transfusions.
‖ This category includes endometritis (inflammation resulting from an infection involving the lining of the womb), pelvic inflammatory disease (involving the nearby reproductive organs such as the fallopian tubes or ovaries), and pelvic infections with sepsis (a serious systemic infection that has spread beyond the reproductive organs). Not included are women with reported sexually transmitted infections such as chlamydia and gonorrhea, cystitis, and toxic shock syndrome not associated with a pelvic infection.
¶ This subset of infections includes cases that were determined to be severe based on medical review of the available case details. Severe infections generally result in death or hospitalization for at least 2-3 days, require intravenous antibiotics for at least 24 hours and total antibiotic usage for at least 3 days, or have other physical or clinical findings, laboratory data, or surgery that suggest a severe infection.

Source: Review by (b) (6) (b) (6) (b) (6) dated 08/27/2015.

D. Ct. ECF No. 28-1 at 88-89.

This table shows a total of 878 women were hospitalized over a 15 year period after taking mifepristone, out of the more than 2.5 million women who had taken the drug at that time. The FDA reviewer explained that:

> [A] few conclusions can be drawn from the information provided:
>
> Given that there have been over 2.5 million uses of Mifeprex by US women since its marketing in 2000, including the use of the proposed dosing regimen and extended gestational age at many clinic/office sites, the numbers of hospitalizations, severe infections, blood loss requiring transfusion and ectopic pregnancy will likely remain acceptably low. The numbers of each of these adverse events appears to have remained steady over time, with a possible decrease in severe infections.

D. Ct. ECF No. 28-1 at 89.

In 2019, Plaintiffs petitioned FDA to rescind certain aspects of the 2016 changes and to "retain the Mifeprex [REMS] and continue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals, by or under the

supervision of a certified prescriber" (2019 petition). D. Ct. ECF No. 1-36 at 2. The 2019 petition did not challenge the 2016 REMS's changes to the dosing requirements or ask FDA to rescind the 2000 approval.

In April 2021, after again reviewing substantial supporting evidence, FDA temporarily suspended the in-person dispensing requirement during the COVID-19 pandemic, explaining that it would exercise enforcement discretion to allow dispensing of mifepristone through the mail or mail-order pharmacies ("2021 non-enforcement order"). FDA's analysis of publications with relevant clinical outcome data was that "the overall findings from these studies do not appear to show increases in serious safety concerns (such as hemorrhage, ectopic pregnancy, or surgical intervention) occurring with medical abortion as a result of modifying the in-person dispensing requirement during the COVID-19 pandemic." D. Ct. ECF No. 1-40 at 2-3.

In December 2021, FDA denied the 2019 petition in large part, in a decision that thoroughly addressed Plaintiffs' concerns, assertions, and sources ("2019 petition denial"). Specifically, FDA declined to undo the challenged 2016 changes and explained that it would exercise enforcement discretion with respect to the in-person dispensing requirement. *See* D. Ct. ECF No. 1-44. FDA granted the 2019 petition insofar as it asked FDA to "retain" the Mifeprex REMS, rather than removing them entirely. D. Ct. ECF No. 1-44 at 41.

FDA also approved a generic version of Mifepristone in 2019.

FDA approved a modified mifepristone REMS on January 3, 2023, which superseded the 2021 non-enforcement decision by lifting the in-person dispensing requirement ("2023 changes").

B. Procedural History

1. In November 2022, Plaintiffs filed suit challenging FDA's actions regarding the 2000 approval, 2002 petition denial, 2016 changes, 2019 generic approval, 2019 petition denial, and 2021 non-enforcement decision under the Administrative Procedure Act (APA). Plaintiffs' claims are based on the Federal Food, Drug, and Cosmetic Act (FDCA), the Comstock Act, the Pediatric Research Equity Act of 2003 (PREA), and FDA's regulations. D. Ct. ECF No. 1. Plaintiffs sought preliminary and permanent injunctive relief.

After FDA approved the modified REMS in January 2023, Plaintiffs did not challenge this action before FDA or in this litigation and did not ask the District Court to enjoin it.

The District Court considered consolidating Plaintiffs' preliminary injunction motion with a merits proceeding under Federal Rule of Civil Procedure 65(a)(2). D. Ct. ECF No. 32. All parties supported the District Court considering the full administrative record before reaching a decision on the merits. D. Ct. ECF Nos. 68, 92, 98. The District Court declined, D. Ct. ECF No. 117, opting instead to render a decision on the preliminary injunction record alone.

On April 7, 2023, the District Court granted Plaintiffs' request for preliminary relief, ordering that "FDA's approval of mifepristone is hereby stayed." App. 109a.

The court held Plaintiffs had standing, could surmount a number of significant barriers to reviewability, and were likely to prevail on the merits of each of their claims. Based on these conclusions, the court "stayed" the 2000 approval, "the 2016 Changes, the 2019 Generic Approval, and the 2021 Actions." *Id.* The court stayed the effect of its order for seven days to allow the parties to obtain emergency relief. *Id.*

The same day the District Court issued its order, the Eastern District of Washington separately enjoined FDA from "altering the status quo and rights as it relates to the availability of Mifepristone under the" January 2023 REMS in the 17 States and the District of Columbia that are plaintiffs in that action. Order Granting in Part Plaintiffs' Motion for Preliminary Injunction at 30, *Washington* v. *FDA*, No. 1:23-cv-03026-TOR (E.D. Wash. Apr. 7, 2023), ECF No. 80.

2. Danco Laboratories and the Government ("Applicants") both sought a stay of the injunction pending appeal in the United States Court of Appeals for the Fifth Circuit. 5th Cir. ECF Nos. 20, 22-1. Plaintiffs opposed the stay motions and also moved to dismiss on jurisdictional grounds. 5th Cir. ECF No. 98.

At midnight on April 12, 2023, the Fifth Circuit issued a per curiam order granting a stay of the injunction order in part and denying it in part, expediting the appeal, and denying Plaintiffs' motion to dismiss. Judge Haynes concurred only in the decision to expedite the appeal and deny the motion to dismiss. She would have granted an administrative stay and deferred the question of whether to stay the District Court's order pending appeal to the merits panel. App. 2a n.*.

First, although Danco and the Government cited *Clapper* v. *Amnesty Int'l USA*, 568 U.S. 398 (2013) and *Summers* v. *Earth Island Inst.*, 555 U.S. 488, 495 (2009) as controlling precedent, the panel concluded Applicants were unlikely to show Plaintiffs lacked individual or associational standing without comparing either case to this one. App. 10a-23a. The panel's standing analysis took unfortunate liberties with the record, including, among other things, selecting portions of quotes that obscured that one declarant was talking about a patient who received drugs online from India and two others were talking about non-personal experience.[3] App. 13a-17a.

Second, the panel agreed Applicants were likely to show that Plaintiffs' challenge to the 2000 approval was untimely because their challenge to the 2002 petition's denial was too late and FDA's later actions did not reopen the 2000 approval. App. 23a-30a. For this reason, the panel granted a stay of the District Court injunction as to the 2000 approval.

Third, the panel concluded Applicants' challenges to the 2016 changes in their 2019 citizen petition and the 2019 generic approval were likely timely and that Applicants were unlikely to succeed on appeal as to those challenges. The panel gave two reasons that Applicants were unlikely to succeed on appeal: (1) "FDA eliminated REMS safeguards based on studies that included those very safeguards," and (2) the 2016 REMS changes had eliminated the heightened requirement to report non-fatal adverse events to FDA. App. 34a–35a. On the first point, the panel complained that

[3] *See* Adam Unikowsky, *Mifepristone and the rule of law, part III*, *available at* https://adamunikowsky.substack.com/p/mifepristone-and-the-rule-of-law-f6a (cataloging the Fifth Circuit's errors in this respect and others).

FDA had studied the changes "in isolation," but faulted FDA for relying on "zero studies that evaluated the safety-and-effectiveness consequences of the 2016 Major REMS Changes as a whole," which the panel said meant FDA had acted unreasonably. App. 34a-35a. The panel identified no requirement in the FDCA or in any regulation imposing this kind of rigid matching requirement where FDA lacks discretion to approve a drug or a change to a drug absent a specific study containing all of the exact parameters that FDA ultimately concludes are appropriate. The panel ignored the substantial evidence for the agency's conclusions found in the dozens of studies involving data on tens of thousands of subjects that FDA analyzed. *See supra* pp. 5-6.

Fourth, the panel found FDA's *2023* REMS modification lifting the in-person dispensing requirement—implemented after this lawsuit was filed—was a final agency action, but did not moot Plaintiffs' challenges to the 2021 non-enforcement decision, and that Plaintiffs' challenge to the 2021 non-enforcement decision was timely and exhausted. App. 6a n.2, 23a, 31a. The court did not address whether Plaintiffs had exhausted any challenge to the 2023 REMS modification, or whether the 2021 non-enforcement decision or 2023 REMS modifications were arbitrary and capricious.

Fifth, the panel concluded the balance of equities did not warrant staying the District Court's order as it pertained to the 2016 changes, 2021 non-enforcement order, or 2023 changes. In the panel's view, it did not matter that Plaintiffs had waited more than twenty years after submitting their citizen petition to file suit. App. 37a-38a. The panel concluded that since it was staying the District Court ruling as to the

2000 approval, there was not sufficient evidence of harms or consequences that would flow from only staying the 2016 REMS modifications and later actions. App. 36a-40a.

The panel also denied Plaintiffs' motion to dismiss for lack of jurisdiction, finding the District Court's "this order would have the practical effect of an injunction because it would remove mifepristone from the market." App. 8a n.3.

The effect of the Fifth Circuit's order, as Danco understands it, is summarized in the following chart:

Agency Action	Reviewability	Merits	Effect
2000 Approval	Untimely, but futile to exhaust in later filings	Not discussed	District Court order stayed; 2000 approval remains in effect
2016 changes	Challenged changes are timely, exhausted	Challenged changes are arbitrary and capricious	District Court order remains in effect; 2016 REMS Modifications stayed
2021 non-enforcement decision	Timely and exhausted; not moot	Not decided	District Court order remains in effect; 2021 non-enforcement decision stayed
2023 REMS Modification	Final agency action; exhaustion not discussed	Not decided	Not raised by Plaintiffs or addressed by District Court; Fifth Circuit suggests it is stayed anyway

Because the Fifth Circuit did not alter the District Court's original stay order, the District Court's order "stay[ing]" the effect of its April 7 injunction for seven days currently remains in effect until the end of today, April 14. *See* App. 109a.

On April 13, 2023, the Eastern District of Washington issued an order "clarif[ying]" that its April 7 injunction preventing FDA from altering the status quo as it relates to the January 2023 REMS applies "irrespective of the Northern District of Texas Court ruling or the Fifth Circuit's * * * ruling." Order Granting Motion for

Clarification at 6, *Washington* v. *FDA*, No. 1:23-cv-03026-TOR (E.D. Wash. Apr. 13, 2023), ECF No. 91.

ARGUMENT

Danco is entitled to a stay pending appeal because (1) Danco is likely to succeed on the merits; (2) Danco will be irreparably injured absent a stay; (3) a stay will not substantially injure other parties; and (4) a stay serves the public interest. *Nken* v. *Holder*, 556 U.S. 418, 434 (2009). Factors one and two "are the most critical." *Id*.

I. DANCO IS LIKELY TO PREVAIL ON THE MERITS.

A. Plaintiffs Lack Standing.

The Fifth Circuit's "unusually broad and novel view of standing," *Valley Forge Christian Coll.* v. *Americans United for Separation of Church & State, Inc.*, 454 U.S. 464, 470 (1982), runs directly against Supreme Court precedent—which is why some of this Court's key decisions make no appearance in the Fifth Circuit's ruling.

"The law of Article III standing, which is built on separation-of-powers principles, serves to prevent the judicial process from being used to usurp the powers of the political branches." *Clapper*, 568 U.S. at 408. To satisfy this constitutional requirement, "a plaintiff must show that (i) he suffered an injury in fact that is concrete, particularized, and actual or imminent; (ii) that the injury was likely caused by the defendant; and (iii) that the injury would likely be redressed by judicial relief." *TransUnion* v. *Ramirez*, 141 S. Ct. 2190, 2203 (2021).

This Court rigorously holds litigants to these requirements. For plaintiffs seeking injunctive relief, "th[e] threatened injury" they allege "must be certainly

impending to constitute injury in fact," *Clapper*, 568 U.S. at 409, meaning an injury that is "sufficiently imminent and substantial," *TransUnion*, 141 S. Ct. at 2210. *Clapper* holds that "allegations of possible future injury are not sufficient." 568 U.S. at 409; *accord City of Los Angeles* v. *Lyons*, 461 U.S. 95, 111 (1983) ("speculative nature of future injury" insufficient). Nor can a plaintiff satisfy Article III by pointing to an "[o]bjectively reasonable likelihood" of injury, "rel[ying] on a highly attenuated chain of possibilities" or "speculat[ing] about 'the unfettered choices made by independent actors not before the court." *Clapper*, 568 U.S. at 410, 414 n.5 (quoting *Lujan* v. *Defenders of Wildlife*, 504 U.S. 555, 562 (1992)). Allegations of past harm are also not enough. *Lyons*, 461 U.S. at 103 ("past wrongs do not in themselves amount to that real and immediate threat of injury necessary to make out a case or controversy"). And that remains the rule even when claims of past harm are coupled with "a statistical probability that some [plaintiffs] are threatened with concrete injury." *Summers*, 555 U.S. at 495, 497.

Plaintiffs also cannot clear the standing bar by alleging harm to other parties, or harm caused by actors other than the defendant. "[T]he party seeking review [must] be himself among the injured." *Lujan*, 504 U.S. at 563; *accord Summers*, 555 U.S. at 493 (no standing where "[t]he regulations under challenge here neither require nor forbid any action on the part of respondents"). Organizational plaintiffs must satisfy all these same requirements. *E.g.*, *Summers*, 555 U.S. 488; *Havens Realty Corp.* v. *Coleman*, 455 U.S. 363, 378-379 (1982).

This Court has long approached standing with circumspection: The doctrine "is not merely a troublesome hurdle to be overcome if possible so as to reach the 'merits' of a lawsuit which a party desires to have adjudicated." *Valley Forge Christian Coll.*, 454 U.S. at 476. If courts ignore "the law of Article III," there is no limit on any "suit against virtually any defendant who violated virtually any federal law." *TransUnion*, 141 S. Ct. at 2206. That result would shred "the basic charter promulgated by the Framers of the Constitution." *Valley Forge Christian Coll.*, 454 U.S. at 476.

On an objective read, Plaintiffs cannot satisfy any of these foundational requirements. They have alleged neither a cognizable injury caused by FDA's actions nor a certainly impending future injury—which is required for injunctive relief. And any injuries they have alleged are not fairly traceable to FDA's 2016 REMS modification or subsequent challenged FDA actions. *See, e.g.*, *TransUnion*, 141 S. Ct. at 2208 ("plaintiffs must demonstrate standing for each claim that they press and for each form of relief that they seek").

1. Plaintiffs have not alleged a "cognizable injury" caused by the 2016 REMS modification or FDA's subsequent challenged actions. This failure dooms their standing claims.

Neither the Fifth Circuit nor the District Court assessed whether Plaintiffs demonstrated injury-in-fact *from the 2016 REMS modification* or the subsequent challenged actions. No declarant linked any asserted past injury to that 2016 REMS modification or even identified if the event had happened before or after that

modification. And both the Fifth Circuit and the District Court's standing analyses seriously misrepresent the statements in Plaintiffs' declarations and overtly rely on a claimed statistical analysis of how likely it is that some unidentified Plaintiff or Plaintiff-member doctor will encounter some unknown patient at some unknown time in the future who was prescribed mifepristone by some other unidentified health care provider and experienced an incomplete treatment or adverse event requiring treatment in the emergency room of some hospital somewhere where the Plaintiff or Plaintiff-doctor member (but probably not the dentists, pediatricians, non-U.S., or retired member doctors among the Plaintiff-associations) would personally perform a follow up surgical abortion.

The Declarations Do Not Say What The Fifth Circuit Attributed To Them. The panel points to a statement about medical treatment by someone in a Plaintiff-physician's "group practice" as treatment by a Plaintiff herself. *Compare* App. 13a, *with* D. Ct. ECF No. 1-9. It attributes a *colleague's* alleged harm to another Plaintiff, and then claims that this proves past harm *to the Plaintiffs*. *Compare* App. 16a-17a, *with* D. Ct. ECF No. 1-8 at 5. The panel recites one declarant's unsupported opinion that the frequency of medication abortions has "increased over time" despite the lack of substantiating facts in the declaration or the statement's conflict with the data in the record. *Compare* App. 15a (opining that the frequency of complications from medication abortion has "increased over time"), *with, e.g.*, D. Ct. ECF No. 1-33 at 22 (FDA concluding that "[t]he established safety profile over 15 years of experience with Mifeprex is well-characterized, stable, and known serious risks occur

rarely."); D. Ct. ECF No. 1-44 at 41 (FDA concluding that "[w]e have not identified any new safety concerns with the use of mifepristone for this indication."); D. Ct. ECF No. 28-1 at 93 (FDA concluding that "no new safety concerns have arisen in recent years").

The Panel's Statistical Mistakes. The court makes significant and obvious statistical errors about both the number of women allegedly suffering rare complications, and the number of physicians who could possibly ever treat those women for the kinds of harms Plaintiffs allege have occurred. First, the court calculates the total number of the 5 million women who have taken mifepristone the label suggests may have had an "unsuccessful" treatment (2-7% of 5 million, or 350,000) and equates that number with how women (a) were directly affected by the 2016 REMS, and (b) necessarily sought out emergency room services. App. 12a-13a. That number is in no universe connected to the 2016 REMS modification. And it is also in no way a 1:1 match with the tiny number of women (far fewer than the 2-7% for whom the treatment is initially incomplete, *see* App. 12a-13a) who have experienced the kinds of side effects or complications from mifepristone after and because of the 2016 REMS modifications that require *emergent medical care*. D. Ct. ECF No. 28-1 at 134-135. Many women return to the clinic or provider that prescribed the medication abortion for a surgical one or additional medication if necessary.

Even assuming that those overblown statistics represent reality, this Court cannot credit the suggestion that any of those women are "statistically certain" to be treated by one of these Plaintiffs. Taking the panel's 350,000 number, divided by 23

years, further divided by the number of emergency rooms (roughly 6,000) and urgent care centers (roughly 9,000) in this country yields approximate one woman per facility per year. This shows why the Court has always held statistics are not a way of showing "certainty." Whatever certainty is, it is more than a fraction of a fraction of a percentage of possibility.[4]

The court also converts the alleged total membership of Plaintiff organizations into a conclusion that *every single member* is an emergency room doctor who faces "inevitabl[y]" treating a woman who has taken mifepristone. App. 18a. That is not a reasonable inference. The Plaintiff-organizations' membership ranks include: (a) doctors who neither practice emergency medicine, nor are ob-gyns, (b) residents of foreign countries, and (c) anyone else who pays the membership fee.[5] Plaintiffs themselves do not contend that each and every one of their members is a doctor, in an emergency room, who treats patients like these hypothetical women.

The Unprecedented Nature of Constitutionally Cognizable Harm. Aided by these rampant factual revisions, the Fifth Circuit transforms the daily realities of medical work into an Article III harm. App. 16a. A doctor's job is to treat patients. That is true regardless of whether the doctor agrees with the patient's choices that have led them to seek medical care (*e.g.*, smoking, legal (or illegal) drugs, poor nutrition, religious abstention from other types of treatments).

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[4] *See* Jonathan Adler, *The Good and the Bad of the Fifth Circuit's Abortion Pill Ruling* (Apr. 13, 2023), *available at* https://reason.com/volokh/2023/04/13/the-good-and-bad-of-the-fifth-circuits-abortion-pill-ruling/.

[5] Adam Unikowsky, *Mifepristone and the rule of law, part III*, *available at* https://adamunikowsky.substack.com/p/mifepristone-and-the-rule-of-law-f6a.

The emotional discomfort associated with providing medical care to a person with whom a physician has a moral, ethical, or religious disagreement is not an Article III injury. *See TransUnion*, 141 S. Ct. at 2200 (Article III injuries must bear a "close relationship" to "a harm traditionally recognized as providing a basis for a lawsuit in American courts"). As Plaintiffs acknowledged to FDA, "[d]rug-induced abortion is optional." D. Ct. ECF No. 1-36 at 12; *see Coalition for Mercury-Free Drugs* v. *Sebelius*, 671 F.3d 1275, 1281 (D.C. Cir. 2012) (Kavanaugh, J.) ("FDA is not forcing [thimerosal-opposed physicians] to administer thimerosal-preserved vaccines, nor is it forcing any patient to receive such vaccines."). Having to "devote" time and resources to care for multiple patients at once is likewise not an Article III injury for emergency room physicians. App. 14a, 19a. It is part of the job.

Plaintiffs' "cognizable injury" argument is just as weak with respect to their organizational standing claims. "[A]n organization does not automatically suffer a cognizable injury in fact by diverting resources in response to a defendant's conduct." *El Paso County* v. *Trump*, 982 F.3d 332, 343 (5th Cir. 2020). Rather, the alleged "diversion" must be in reaction to the challenged conduct, significantly and "perceptibly impair[]" the organization's mission, and have a "consequent drain on the organization's resources." *Havens*, 455 U.S. at 379; *accord NAACP* v. *City of Kyle*, 626 F.3d 233, 238 (5th Cir. 2010). A "simpl[e]* * * setback to the organization's abstract social interests," *Havens*, 455 U.S. at 379, or conduct that does not "differ from [the organization's] routine activities." will not suffice, *El Paso County*, 982 F.3d at 344.

The Fifth Circuit opined that "FDA's actions have frustrated [Plaintiff organizations'] organizational efforts to educate their members and the public on the effects of mifepristone." App. 22a. Yet every "harm" Plaintiffs identified falls into their organizations' conceded "duties and responsibilities." D. Ct. ECF No. 1-4 at 4,7; D. Ct. ECF No. 1-5 at 5-7. For example, Plaintiff-organizations avow that they are "morally and ethically opposed to *all forms of* abortion," D. Ct. ECF No. 1-4 at 4. So "for decades," they have routinely brought challenges to abortion access and outreach about the "dangers" of abortion-related healthcare. D. Ct. ECF No. 7 at 7. This balancing act between multiple organizational priorities—all of which serve one goal—is not a "diversion" of resources and is insufficient for standing. *See, e.g.*, *El Paso County*, 982 F.3d at 344. As a result, there is no "causal connection between the injury and the conduct complained of"—and organizations can no more escape the traceability requirement than individuals. *See City of Kyle*, 626 F.3d at 237; *Tenth Street Residential Ass'n* v. *City of Dallas*, 968 F.3d 492, 499 (5th Cir. 2020).

2. No Plaintiff's declaration shows that he or she faces a "certainly impending" future injury: they lack basic information about when or where any injury would occur, let alone how it would be linked to the 2016 REMS modification. In *Clapper*, this Court reversed the Second Circuit's use of an "objectively reasonable likelihood" standard and explained that because the statute at issue there "at most authorizes—but does not mandate or direct" a particular action, an allegation of harm from an independent actor's discretionary action is "necessarily conjectural." *Clapper*, 568 U.S. at 412. The Fifth Circuit's decision embraces the reasoning this Court rejected

in *Clapper*—which is why the panel never tries to square its decision with *Clapper*'s reasoning, holding, or analysis.

Pointing to past incidents, as the panel did, is no substitute for concrete, impending future injury that is personal to a specific plaintiff. *Summers*, 555 U.S. at 495; *Lyons*, 461 U.S. at 103. As then-Judge Kavanaugh explained, "[e]ven if a plaintiff has suffered past harm from the kind of conduct the suit seeks to enjoin, the plaintiff must 'establish a real and immediate threat' that the harm-producing conduct will recur." *Coalition for Mercury-Free Drugs*, 671 F.3d at 1278-80. For precisely that reason, Plaintiff-physicians' statements that they (or a colleague, or some other doctor they know) previously treated a woman for complications related to medication abortion cannot excuse their failure to show a sufficiently imminent, non-speculative, non-statistical personal risk of future harm—and certainly not one linked to the 2016 REMS modifications that they seek to undo. *See Clapper*, 568 U.S. at 409 ("[T]hreatened injury must be *certainly impending* to constitute injury in fact.") (emphasis in original).

Plaintiffs offered no facts showing a "real and immediate threat" of future harm from the 2016 REMS modification. Their allegations of future harm amount to nothing more than a general statistical possibility that out of the universe of all women who may seek a medication abortion, one of their physician-members will be "forced" to treat such a woman sometime, somewhere. D. Ct. ECF No. 7 at 7-8; Op. 15. The Fifth Circuit converts this possibility into a certainty based on statements about past incidents involving a small number of circumstances of some emergency

room doctor providing a surgical abortion for an incomplete medication abortion—none of which, to say it again, is linked to the 2016 REMS modification—and misrepresents the "Patient Agreement Form" as providing "statistical certainty" that Plaintiffs will need to provide emergency care after a medication abortion. App. 17a-18a. But this Court has said that past harm is proof of future harm.

Even on past harm, Plaintiffs' declarations are lacking: they claim FDA's decisions to no longer require in-person dispensing by a physician raises the risk that someone with an ectopic pregnancy will take mifepristone and come to them for emergency care. But no Plaintiff says that he or she *has ever treated a single patient who had an ectopic pregnancy and took mifepristone*—not once—either before or after the in-person dispensation requirements were lifted. Further undercutting any statistical certainty, the District Court's own source (at App. 95a n.52) shows that there have only been 97 instances of ectopic pregnancies out of the millions of women who have had medication abortions. FDA, *Mifepristone U.S. Post-Marketing Adverse Events Summary Through 6/30/2022*, https://www.fda.gov/media/164331/download.

The Fifth Circuit concluded that "even if one of the named doctors never sees another patient, it's *inevitable*" that some other unidentified doctor-member of the plaintiff associations will." App. 18a (emphasis added). The majority opinion in *Summers* made short work of that notion, characterizing the *Summers* dissenters' willingness to find standing based on a statistical probability as "mak[ing] a mockery" of this Court's standing doctrine. *Summers*, 555 U.S. at 498-499. Such hypothetical reasoning is "pure speculation and fantasy." *Lujan*, 504 U.S. at 567; *see also Public Citizen,*

Inc. v. *National Highway Traffic Safety Admin.*, 489 F.3d 1279, 1294 (Kavanaugh, J.) (D.C. Cir. 2007) ("[T]here is a powerful argument that 'increased-risk-of-harm' claims–such as [Plaintiffs'] claim here–fail to meet the constitutional requirement that a plaintiff demonstrate harm that is 'actual and imminent, not conjectural or hypothetical.'").

3. Plaintiffs' asserted injuries also are not "fairly traceable" to FDA's 2016 REMS modification or later challenged decisions. None of those decisions directly regulates Plaintiffs. Just as in *Summers*, the agency "neither require[s] nor forbid[s] any action on the part of respondents." *Summers*, 555 U.S. at 493. FDA's regulations become relevant to Plaintiffs only after a chain of decisions by independent actors. Physicians who prescribe mifepristone *may* do so in person or by telemedicine. Those physicians *may* disclose the potential side effects and contraindications to their patients. Patients who consult with those physicians *may* determine that medication abortion is a preferable course of treatment for them. If they choose medication abortion, those same patients *may* decide that they wish to take the drug regimen at home, rather than in their physician's office. If they experience side effects, those patients *may* go to an emergency room as opposed to consulting with their prescribing physician or other women's medical center.

It is only at the end of this chain of third-parties' discretionary decisions that Plaintiffs make an appearance. Even then, to find a link to Plaintiffs, the panel must say that "women who use this drug *cannot possibly* go back" to the prescriber, App. 13a (emphasis added), so they "*must*" seek emergency-room care. App. 19a. That is

flatly not true. The language of the very Provider Agreement cited by the Fifth Circuit one page earlier shows the fallacy. It says that the patient agrees to talk to the prescribing provider about a surgical procedure and that the provider will tell the patient "*whether they will do the procedure* or refer me to a provider who will." App. 12a (emphasis added). In this case, as in every case, "theories that require guesswork as to how independent decisionmakers will exercise their judgment" are insufficient to establish standing. *See Clapper*, 568 U.S. at 413; *see also Arpaio* v. *Obama*, 797 F.3d 11, 15 (D.C. Cir. 2015) ("[S]tanding based on third-party conduct * * * is significantly harder to show than standing based on harm imposed by one's litigation adversary. That difficulty is compounded here because the third-party conduct * * * depends on large numbers of people having the same unlikely experiences and behaviors.").

B. Plaintiffs Lack Any Viable Merits Claims.

The Fifth Circuit embraced the most troubling aspect of the District Court's analysis: that FDA's approval of NDA, sNDAs, or labeling changes requires a clinical study containing every element in exactly the format that will govern the approved use of the drug. Having multiple clinical trials that study different aspects of a drug's safety and efficacy is insufficient to allow for reasoned scientific decisionmaking, the panel says, so there must be one clinical trial conducted under the exact terms—"as a whole"—that will appear in the approved use. App. 35a; *see also* App. 91a-92a, 101a-102a.

The law requires no such thing. Before approving a new drug, FDA is required to evaluate whether there is "substantial evidence" of effectiveness from "adequate and well-controlled investigations" and sufficient evidence of safety, and evaluate whether the drug's benefits outweigh any risks. 21 U.S.C. § 355(d); *see also* FDA, *Draft Guidance for Industry: Benefit-Risk Assessment for New Drug and Biological Products* at 3 (Sept. 2021) ("Because all drugs can have adverse effects, the demonstration of safety requires a showing that the benefits of the drug outweigh its risks."). To modify a REMS, FDA must determine if there is an "adequate rationale" that such modifications would ensure that the benefits of the drug would outweigh the risks, while minimizing burden on the healthcare system. 21 U.S.C. § 355-1(g)(4)(B); *see also* 21 U.S.C. § 355-1(f)(2). In considering a REMS, FDA is not limited to just clinical trials; it can also consider postapproval studies, adverse event reports and other postmarket safety data, and peer-reviewed scientific literature. *See* 21 U.S.C. § 355-1(b)(3). The statutory language makes clear that Congress intentionally provided flexible standards, rather than stringent and circumscribed limitations, to allow FDA to extrapolate from the various data sources put before it. As a result, no exact match is required for either new drug approvals or for REMS modifications.

The consequences of the court's freelancing cannot be overstated: Over 150 pharmaceutical companies, executives and investors told the Fifth Circuit that under this "groundless approach, it is unlikely that a single [drug] would have been approved—or that their approvals would have gone unchallenged—and countless patients would have suffered needlessly." Pharmaceutical Companies' Amicus Br., 5th

Cir. ECF No. 118 at 34-37. Applying this regulatory sea-change going forward injects instability into the entire pharmaceutical industry, stifles industry innovation, and will delay critical care for patients by effectively precluding any drug approval. FDA regularly requires more limitations in clinical trials than ultimately appear on the label. For good reason: trials are often designed to determine what conditions are, and are not, necessary to include in a label when the drug goes to market. *See id.* at 22-25. But under the panel's reasoning, drug developers must conduct an additional time-consuming and expensive trials on its exact proposed conditions of use, or risk endless challenges to drug approval. This judicially created requirement would stifle innovation on current and future drugs. Changes to the label of approved drugs are often supported by multiple types of studies and data. Requiring clinical trials with a one-to-one match of all labeling changes would impose a costly and unjustified burden. Pharmaceutical Companies' Amicus Br., 5th Cir. ECF No. 118 at 30-31. Every drug approval will be subject to second-guessing by courts, which will effectively upend the finality of a drug approval. The consequences will fall most heavily on patients, who could be deprived access to critical care or miss out on improvements to existing treatments.

C. The 2023 Changes Were Not Before The Fifth Circuit.

Plaintiffs did not—and could not—have included a challenge to the 2023 REMS modification in their complaint. They filed suit before it was approved, *see* D. Ct. ECF No. 1, and then chose not to amend their complaint, raise it in their briefing after the modification issued, or talk about it in their Fifth Circuit briefing, *see* D. Ct.

ECF Nos. 68, 120; 5th Cir. ECF No. 47. The District Court limited its rulings to the "challenged actions," which stopped with FDA's 2021 actions. App. 107a.

The Fifth Circuit's opinion, however, goes further; it suggests that it also "stay[ed]" the 2023 REMS modifications. App. 2a. In a footnote, the panel concluded that it had authority to review the 2023 changes because "[t]he Supreme Court has explicitly instructed this court to review a new agency action finalized after litigation commenced and while the appeal was pending because this decision was a 'final agency action.'" *Id.* at 6 n.2 (citing *Texas* v. *Biden*, 142 S. Ct. 2528 (2022)). But the facts of *Texas* v. *Biden* are far afield from this case. There, the district court *remanded* the challenged action to the agency; while the appeal was pending, the agency issued a revised opinion supplementing its prior decision. *See id.* at 2536-37. That process essentially rendered the new opinion a part of the existing case.

Here, the 2023 REMS update occurred before the *District Court* had even ruled: The obvious path to placing that action before the court was a Rule 8 amendment to Plaintiffs' complaint. If they had, Danco would have explained that the 2023 REMS modification did more than simply replace the 2021 non-enforcement decision; it discretely modified several dispensation requirements unrelated to the drug's underlying approval. The Fifth Circuit overstepped by purporting to keep an injunction in place as to the 2023 REMS modifications that the District Court never said it was enjoining in the first place.

II. THE EQUITIES OVERWHELMINGLY FAVOR A STAY.

The harm to Danco and the public interest from the failure to grant a stay overwhelmingly favor a stay and significantly outweigh any speculative injury to Plaintiffs.

Without waiting for the administrative record or considering whether remand without vacatur would apply here, the court issued a mandatory injunction upending a decades-old drug approval. A mandatory injunction that purports to "reinstate" a prior state of affairs is an "extraordinary remedy to be employed only in the most unusual case." *Communist Party of Ind.* v. *Whitcomb*, 409 U.S. 1235, 1235 (1972) (Rehnquist, J., in chambers); *Barthuli* v. *Bd. of Trustees of Jefferson Elementary Sch. Dist.*, 434 U.S. 1337 (1977) (Rehnquist, J., in chambers); *accord, e.g.*, *Martinez* v. *Mathews*, 544 F.2d 1233, 1243 (5th Cir. 1976) ("Mandatory preliminary relief, which goes well beyond simply maintaining the status quo," "is particularly disfavored."). Upending what has been the status quo since the 2016 REMS modification is the wrong remedy when "[t]here is a serious possibility" that FDA could remedy any concerns and "the disruptive consequences of vacating are substantial." *Apache Corp.* v. *FERC*, 627 F.3d 1220, 1223 (D.C. Cir. 2010) (Kavanaugh, J.).

Neither the District Court nor the Fifth Circuit addressed the heightened standard for a mandatory injunction. But there is no reasonable debate that the injunction here would—and was intended to—disrupt the longstanding status quo. In fact, Plaintiffs admitted they sought a mandatory injunction. D. Ct. ECF No. 7 at 23.

A. Danco Faces Substantial, Certain, Unrecoverable Harm.

The Fifth Circuit's order creates debilitating uncertainty for Danco that threatens its very existence. The court's ruling implies that it "stays" the 2023 REMS modifications, even though those were not before it, and returns to the pre-2016 world, even though another district court has prohibited FDA from changing the current state of affairs in 17 states and the District of Columbia. App. 111a ¶ 6. The result is a regulatory mess that will irreparably injure Danco by making it exceedingly difficult, if not impossible, for Danco to continue selling its only product. *See Wages & White Lion Invs., LLC* v. *FDA*, 16 F.4th 1130, 1142 (5th Cir. 2021) (economic harms indisputably irreparable when the "alleged financial injury threatens the very existence of [the movant's] business") (internal quotation marks omitted).[6]

1. The Fifth Circuit's order, standing alone, will irreparably injure Danco. In order to distribute Mifeprex under something other than the 2023 REMS, Danco must: revise product labels, packaging, and promotional materials; recertify providers; and amend its supplier- and distributor-contracts and policies (among other things). App. 113a ¶ 11-12. All of these are currently based on the 2023 REMS. App. 115a ¶ 17. So is Danco's current distribution model. App. 115a ¶ 18. Before Danco can make any changes, however, it must have a new REMS—which will require Danco to submit and FDA to approve a supplemental NDA (sNDA). App. 119a ¶ 26.

[6] The Fifth Circuit faulted Danco for not specifically addressing the harms and complexities that would result from a *partial* stay of the District Court's order. *See* App. 37a, 40a. Danco focused predominantly on the harms flowing from the District Court order because it sought a stay of the District Court order. Nevertheless, many of the arguments presented to that court apply to a stay of the 2016 REMS and subsequent FDA actions for the reasons explained herein.

That process typically takes months. *Id.* It is unclear whether Danco can continue distributing Mifeprex while that sNDA is pending before FDA even though it would technically be misbranded, or whether doing so would expose Danco to civil and criminal penalties. *See* App. 113a-114a ¶¶ 12, 15, 118a ¶ 24(d). And then Danco might be required to jump through all of these hoops *again* if the injunction is ultimately modified or rescinded on appeal. App. 120a ¶ 27.

In the face of this uncertainty, Danco may well be forced to halt operations. *See* App. 115a ¶¶ 17, 18, 117a ¶ 22, 119a-120a ¶ 26. Even if Danco were able to resolve all of these questions and continue operating under the terms of the Fifth Circuit's order, the order would substantially disrupt Danco's operations because it cannot make these changes before the stay of the District Court's order expires today. App. 117a ¶ 23.

2. Then there is the dueling injunction from the Eastern District of Washington. The Washington court's order prohibits FDA from approving any changes to the 2023 REMS in 17 states and the District of Columbia. That puts Danco in an impossible position. Danco cannot comply with the Fifth Circuit's order *unless* FDA approves an sNDA; the Washington court's order *prohibits* FDA from approving that sNDA, at least as to almost half the country. FDA cannot permit Danco to simultaneously operate two separate distribution networks for two different parts of the country; that simply is not how the federal regulation of pharmaceuticals works. App. 116a-117a ¶ 21. The result: Danco will either have to stop distributing Mifeprex as currently labeled to approximately half the country–which will fundamentally

threaten its business and continued existence, not to mention functionally eliminate access to medication abortion in those states. Or Danco will have to continue distributing Mifeprex in half the country in a way that complies with only one of the two court orders–exposing itself to potential fines, sanctions, and other penalties. App. 114a ¶ 14. Either one constitutes irreparable injury. *Morales* v. *Trans World Airlines, Inc.*, 504 U.S. 374, 381 (1992) (party's "Hobson's choice" between "expos[ing] themselves to potentially huge liability" or "suffer[ing] the injury of obeying the law during the pendency of the proceedings" was irreparable harm); *Wages & White Lion Invs., LLC*, 16 F.4th at 1142.

B. The Public Interest Favors A Stay.

A stay decidedly serves multiple aspects of the public interest, including: the biopharmaceutical industry, other regulated entities that touch medication abortion, the States and the separation-of-powers, women, and the healthcare system.

Start with the biopharmaceutical industry writ large. The District Court's newly fabricated, unbounded legal standard that FDA acts arbitrarily and capriciously when the conditions of use approved a drug label do not match the conditions in the clinical trials supporting approval already threatened to throw the industry into disarray. *See generally* Pharmaceutical Companies' Amicus Br., 5th Cir. ECF No. 118. The Fifth Circuit's order makes that untenable situation even worse: The District Court's opinion at least left open the option of mixing-and-matching studies and conditions. But under the Fifth Circuit's logic, FDA cannot approve a drug unless it relies on a *single study* that evaluated the drug under the *exact* conditions

approved. App. 35a. No drug that is currently on the market would meet that test. *See* Pharmaceutical Companies' Amicus Br., 5th Cir. ECF No. 118 at 19, 22-23; *id.* at 11, 15 (explaining why "flexibility is crucial" in clinical studies, and that "clinical trials are not intended to perfectly mirror real-world conditions").

As *nearly 700* members of the industry have explained, "[a]dding regulatory uncertainty to the already inherently risky work of discovering and developing new medicines" and "will likely have the effect of reducing incentives for investment." *See* Letter Petition in Support of FDA's Authority to Regulate Medicines (Apr. 7, 2023). "And without necessary investment, drug development would freeze, stifling innovation," and "caus[e] widespread harm to patients, providers, and the entire pharmaceutical industry." Pharmaceutical Companies' Amicus Br., 5th Cir. ECF No. 118 at 3, 24.

The Fifth Circuit's order also inflicts uncertainty around the country. Unless the Court stays the Fifth Circuit's decision, tomorrow will mark the beginning of an unheralded period of national uncertainty over the legal conditions governing medication abortion. The injunction leaves manufacturers, suppliers, distributors, and prescribers without statutory or regulatory guidance as to the effect of the Order. *See* App. 116a ¶ 20, 119a ¶ 25. They too will be caught between the same rock and hard place as Danco as a result of the dueling preliminary injunctions and confusion surrounding the Fifth Circuit's order—and could potentially also face criminal liability, or civil fines as a result. *See* App. 118a ¶ 24(d). To take but a few examples, it is unclear: what labels and packaging Danco should use for Mifeprex; whether suppliers

and distributors can ship Mifeprex that complies with the 2023 labels to certain states or no states; and whether providers need to use the 2016 or the 2023 Patient Agreement Form to obtain informed consent when prescribing Mifeprex. Indeed, Danco has already received numerous questions from certified prescribers and healthcare settings about the scope of the Fifth Circuit's order—questions Danco is unable to answer. App. 116a ¶ 20.

The lower courts' orders also harm the States' sovereign interests and the separation-of-powers. *Dobbs* consciously "returned the issue of abortion to the people's elected representatives." *Dobbs* v. *Jackson Women's Health Org.*, 142 S. Ct. 2228, 2243 (2022). The injunction eviscerates that sovereign authority for States that "wish to protect rather than restrict abortion access," *see* New York et al. Amicus Br., 5th Cir. ECF No. 52-1 at 3, 8; imposes "heightened health and economic costs" on local governments, *see* Local Governments' Amicus Br., 5th Cir. ECF No. 141 at 1-2; burdens already overwhelmed public hospital systems, *see* City of New York et al. Amicus Br., 5th Cir. ECF No. 114 at 25-33; and upsets Congress's decision to assign FDA responsibility for safety and efficacy determinations, which courts review for substantial evidence and with significant deference, *see* 240 Members of Congress Amicus Br., 5th Cir. ECF No. 110 at 4-8.

Absent a stay, women will be seriously and irreparably harmed by the Fifth Circuit's order. The panel majority dismissed these concerns out of hand, finding that the 2016 REMS "and subsequent FDA activity" could not be "critical to the public given that the Nation operated—and mifepristone was administered to millions of

women—without them for sixteen years following the 2000 Approval." App. 40a. Nothing could be further from the truth.

As a direct result of the opinions below, women face serious health risks and the denial of access to essential medical care. If FDA cannot approve the changes to the REMS required to comply with the Fifth Circuit's order because of the Washington injunction, Danco will be unable to distribute Mifeprex—either in the 33 states not covered by Washington's order, or nationwide in the event that the Fifth Circuit's order governs. App. 114a ¶¶ 13-14. That will result in a complete loss of medication abortion access to millions of women, even if their individual circumstances make them a better candidate for a medication abortion than a surgical abortion. 5th Cir. ECF No. 29 at 71-72 ¶¶ 10-11 (Goldberg Declaration), 86-87 ¶¶ 17-20 (Schreiber Declaration). Many patients will be pushed to a surgical abortion at a later gestational age given limited availability, or to unapproved regimens with a lower complete success rate and more intense side effects. 5th Cir. ECF No. 29 at 72-73 ¶¶ 13-14 (Goldberg Declaration), 84 ¶ 12, 87-88 ¶¶ 21-22 (Schreiber Declaration). Preventing doctors from exercising their medical judgment as to the best course of treatment for particular patients and restricting women's access to the standard of care for medication abortion while appellate review plays out will inflict irreparable physical and psychological harm on large numbers of women. 5th Cir. ECF No. 29 at 73 ¶ 15 (Goldberg Declaration), 87-88 ¶¶ 19, 21 (Schreiber Declaration).

Even if Danco is able to obtain a new sNDA at some point, it will not be able to do so before the injunction expires later today, meaning this loss of access is

inevitable for at least some period. App. 117a ¶ 23; App. 120a ¶ 27 (explaining sNDA process "can be expected to take months, at the very least"); App. 113a ¶ 12 (explaining numerous activities that must occur after FDA approval, but before Danco can distribute Mifeprex under a new REMS). And by that point, the harms to Danco from inability to distribute its sole product may have led the company to shutter—permanently ending access for women everywhere. *See* App. 117a ¶ 23.

And *even if* Danco is willing and able to continue operating long enough to return to the pre-2016 world, that will *still* cause significant harm to women by increasing barriers to access. *See* App. 116a-117a ¶ 21. The Fifth Circuit's contrary opinion assumes that the world exists exactly as it did in 2000; but since *Dobbs*, many abortion clinics have shuttered, significantly increasing travel and wait times for remaining clinics. *See, e.g.*, New York et al. Amicus Br., 5th Cir. ECF No. 52-1 at 11-12; Members of Congress Amicus Br., 5th Cir. ECF No. 110 at 2-3. Some women will thus be forced to make an untenable choice: travel hundreds of miles, multiple times, and risk losing one's job; see a surgical abortion instead of medication abortion—which has limitations of its own; or carrying an unwanted pregnancy, with all the attendant consequences. *See, e.g.*, New York et al. Amicus Br., 5th Cir. ECF No. 52-1 at 9-10; Members of Congress Amicus Br., 5th Cir. ECF No. 110 at 19-21.

These consequences will ripple across the entire healthcare system, too. Medication abortion *reduces* the burdens on our healthcare system. Staying or suspending its approval, in whole or in part, "threaten[s] to overwhelm" those systems, as increased demand for both in-person appointments to obtain medication abortion and

surgical abortion will limit the availability of other critical health care services the same physicians provide, such as pre- and post-natal care, contraceptive care, and cancer screening. New York et al. Amicus Br., 5th Cir. ECF No. 52-1 at 12-13; Medical & Public Health Societies Amicus Br., 5th Cir. ECF No. 111 at 5. Already-strained medical facilities in many communities simply do not have the resources to treat the influx of patients who would otherwise safely and effectively complete the FDA-approved regimen at home. Medical & Public Health Societies Amicus Br., 5th Cir. ECF No. 111 at 21. These are the on-the-ground consequences of judicial interposition into the drug regulatory regime.

If that were not enough reasons, here is one more: These disruptive consequences would never have occurred if the District Court had consolidated the preliminary injunction hearing with the merits, as all parties agreed it should. 5th Cir. ECF Nos. 68, 92, 98. For even if Plaintiffs prevail on the merits, the appropriate remedy in this case would be remand without vacatur to allow FDA to consider and remedy any issue with its decisionmaking that the court identifies. *Cent. & S. W. Servs., Inc.* v. *EPA*, 220 F.3d 683, 692 (5th Cir. 2000). That is particularly true here, given "the disruptive consequences of an interim change that may itself be changed." *Allied-Signal, Inc.* v. *U.S. Nuclear Regul. Comm'n*, 988 F.2d 146, 150–51 (D.C. Cir. 1993). A preliminary injunction cannot award a party more relief than would be available on the merits, *see De Beers Consol. Mines* v. *United States*, 325 U.S. 212, 220 (1945)—but that is exactly what the District Court and the Fifth Circuit effectively did,

causing significant disruption, harm, and uncertainty in the process. A stay will serve the public interest.

C. Plaintiffs Face No Irreparable Harm From A Stay.

On the other side of the scale, *no* harm will flow to Plaintiffs from a stay. The Fifth Circuit's order leaves mifepristone on the market so the only question is whether Plaintiffs substantiated any harms they personally face, imminently and irreparably, as a result of the 2016 REMS modification. Plaintiffs have not, and cannot, contend that the harms they allege can be attributed to those regulatory changes alone. *See* D. Ct. ECF No. 7 at 24-25; D. Ct. ECF No. 120 at 23-24; 5th Cir. ECF No. 92 at 45.

Plaintiffs' dilatory actions confirm as much: Plaintiffs took nearly a full year to file suit after FDA denied their 2019 citizen petition—and then proposed a schedule that would have delayed any merits ruling by several months. *See* ECF No. 68. The Fifth Circuit did not explain why Plaintiffs' delay does not undermine any claims of irreparable injury. *See Benisek* v. *Lamone*, 138 S. Ct. 1942, 1944 (2018) (per curiam) ("party requesting a preliminary injunction must generally show reasonable diligence").

In any event, the Fifth Circuit's conclusions on harm to Plaintiffs are wrong for the same reasons its conclusions on standing are wrong: Plaintiffs allege speculative concerns about rare instances of follow-up care stemming from third-party discretionary actions. That is not irreparable harm. *See Google, Inc.* v. *Hood*, 822 F.3d 212, 228 (5th Cir. 2016) (requiring "imminent, non-speculative irreparable injury");

supra pp. 24-26. Even if Plaintiffs' purported harms were present in the record or grounded in fact, such small numbers of speculative future injuries pale in comparison to the certain injuries to the public and Danco that will result absent a stay. A stay of the entire District Court order is warranted.

CONCLUSION

This Court announced in *Dobbs* that it was returning the issue of abortion to the political branches. 142 S. Ct. at 2243. If the Court denies a stay, it abandons that assurance. Allowing the Fifth Circuit's opinion to stand eviscerates the sovereign authority of States that wish to expand and protect access to medication abortion in their jurisdictions. The Court should enter an administrative stay and stay the preliminary injunction pending appeal. Alternatively, the Court should grant certiorari before judgment and set this case for expedited briefing and argument before the summer recess.

Respectfully submitted,

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