IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

BELLA HEALTH AND WELLNESS et al., *Plaintiffs*, CHELSEA M. MYNYK, *Plaintiff-Intervenor*, v. PHIL WEISER, in his official capacity as Attorney General of Colorado, et al., *Defendants*.	Case No. 1:23-cv-939-DDD-SKC

EXPERT REPORT OF
MONIQUE CHIREAU WUBBENHORST, M.D., M.P.H.

I, Monique Chireau Wubbenhorst, pursuant to 28 U.S.C. § 1746, hereby declare as follows:

1. I am a practicing board-certified obstetrician-gynecologist with over 30 years' experience in patient care, teaching, research, health policy, public health, global health, and bioethics. I graduated from Mount Holyoke College and received my medical degree from Brown University and my master's degree in public health from Harvard University. I completed my residency in Obstetrics and Gynecology at Yale-New Haven Hospital and my postdoctoral fellowship in health services research at the Sheps Center for Health Services Research at the University of North Carolina-Chapel Hill. I joined the faculty at the Duke University School of Medicine in the Department of Obstetrics and Gynecology in 2003, a position I held until 2018. While

at Duke I was a member of the Duke Institutional Review Board (IRB) for 15 years. I subsequently served as Senior Deputy Assistant Administrator in the Bureau for Global Health at the United States Agency for International Development. I am currently a Senior Public Policy Fellow at the De Nicola Center for Ethics and Culture at the University of Notre Dame. I also serve as a visiting consultant in Obstetrics and Gynecology at Tenwek Mission Hospital in Bomet, Kenya. I am licensed to practice medicine in North Carolina and Indiana and am certified by the American Board of Obstetrics and Gynecology, a certification I have held since 1997.

2. My clinical career has focused on caring for women in underserved and disadvantaged populations, especially African American and Native American communities, with a focus on women with medical, social, and psychiatric comorbidities. I have worked in multiple domestic and international contexts, including inner-city Boston, rural North Carolina, the Veterans Administration, and Native American reservations, as well as in Kenya, India, the Philippines, Kazakhstan, Ghana, South Sudan, Uganda, Nepal, and Cameroon.

3. I am a fellow of the American College of Obstetricians and Gynecologists and a fellow of the American Heart Association. I have authored over 20 peer-reviewed publications and have been a reviewer for peer-reviewed journals including *The British Journal of Obstetrics and Gynecology*, *Public Health*, *The Journal of Medical Ethics*, *PLOS One*, *Journal of General Internal Medicine*, *Public Health*, *Issues in Law and Medicine*, and *The North Carolina Medical Journal*. My research interests in-

clude the epidemiology and molecular biology of adverse pregnancy outcomes and reproductive health, health services research, racial-ethnic disparities in women's health, adverse pregnancy outcomes and long-term cardiovascular health, maternal mortality, women veterans' health, and ethics in epidemiology and reproductive health.

4. My experience, qualifications, and prior publications are set forth in further detail in my curriculum vitae, which is attached hereto as Exhibit 1.

5. I have been asked by Plaintiffs to opine regarding *Bella Health and Wellness v. Weiser*, No. 1:23-cv-939-DDD-SKC, a legal action challenging the constitutionality of SB 23-190, a Colorado law that bans providing or publicizing abortion pill reversal. I am being compensated at a rate of seven hundred dollars ($700.00) per hour worked, and I will be compensated at the same rate per hour for any testimony given.

6. The opinions I express in this declaration are based on my education, training, experience, and ongoing familiarity with medical literature. These opinions are my own and do not represent the opinion of my employer or of any professional or other group.

OPINIONS

I. There is scientific evidence that supports the clinical use of progesterone to counteract the effects of mifepristone.

7. There are multiple lines of scientific evidence that support the use of progesterone to attempt to reverse the abortifacient action of mifepristone. These include, but are not limited to, the biochemistry of progesterone and its role in female fertility

and pregnancy; studies on progesterone's effectiveness in treating threatened miscarriage; basic science evidence about how mifepristone works and the interactions between a receptor antagonist and receptor agonist; animal studies indicating that progesterone can counteract the effects of mifepristone; and reports on the use of progesterone following the administration of mifepristone for abortion.

A. Progesterone and its role in female fertility and pregnancy

8. To understand how abortion pill reversal works, it is necessary to begin with the biochemistry of progesterone.

9. Progesterone is a naturally occurring hormone, so named because it promotes gestation, among other functions.[1] It plays an essential role in regulating the reproductive function of the uterus, ovaries, mammary glands, and brain, and is particularly critical to achieving and maintaining a healthy pregnancy.[2]

10. During the first ten weeks of pregnancy, progesterone is secreted by a highly specialized structure in the ovary (the corpus luteum), which forms after ovulation and is the main source of progesterone while the placenta develops. Once the placenta has grown to a certain size, it is the main source of progesterone during the remainder of pregnancy.[3]

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[1] *See* W. M. Allen et al., *Nomenclature of Corpus Luteum Hormone*, 136 Nature 303, 303 (1935) (discussing identification of the "progestational hormone") (Exhibit 2).

[2] *See generally* Lucie Kolatorova et al., *Progesterone: A Steroid with Wide Range of Effects in Physiology as Well as Human Medicine*, 23 Int'l J. Molecular Scis. 7989 (2022) (Exhibit 3).

[3] Jessie K. Cable & Michael H. Grider, *Physiology, Progesterone*, StatPearls Publishing (2022) (Exhibit 4).

11. Progesterone binds to the progesterone receptor in cells, and when it does, specific pathways are activated. Among other things, progesterone stimulates the formation of glands in the endometrium (the lining of the uterus), preparing it for the implantation of the developing embryo (blastocyst).[4] It also stimulates the endometrium to produce glucose, proteins, and other nutrients that support the developing embryo. In late pregnancy, progesterone plays a role in the relaxation of smooth muscle, promoting uterine relaxation prior to delivery.[5]

12. Bioidentical progesterone, which is synthesized from steroid precursors, has the same chemical structure as naturally produced progesterone and has been used to support female fertility in a variety of ways for more than 50 years.[6] There are numerous and well-known indications for progesterone therapy in both obstetrics and gynecology, including treatment of recurrent miscarriages, prevention of preterm birth, treatment of secondary amenorrhea (lack of menstrual cycles), treatment of excessive blood loss during menstruation, treatment of premenstrual syndrome, hormonal therapy after surgical or natural menopause, and prevention and treatment of endometrial hyperplasia (thickening of the uterine lining).[7] Notably, progesterone is

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[4] *See* Arri Coomarasamy et al., *PROMISE: first-trimester progesterone therapy in women with a history of unexplained recurrent miscarriages – a randomised, double-blind, placebo-controlled, international multicentre trial and economic evaluation*, 20 Health Tech. Assessment, May 2016, at 1 (Exhibit 5).

[5] *See* N.E. Simons et al., *The long-term effect of prenatal progesterone treatment on child development, behaviour and health: a systematic review*, 128 BJOG: Int'l J. Obstet. & Gyn. 964, May 2021 (Exhibit 6).

[6] *See* Gian Carlo Di Renzo et al., *Progesterone: History, facts, and artifacts*, 69 Best Practice & Rsch. Clinical Obstetrics & Gynaecology 2 (2020) (Exhibit 7).

[7] *See* Kolatorova et al., *supra* note 2.

routinely used to treat luteal phase defect (LPD), a type of infertility, and is also used as part of in vitro fertilization (IVF) protocols, where it is part of routine care to both support endometrial function and help prevent miscarriage.

13. All uses of supplemental progesterone except for treatment of endometrial hyperplasia (pathological thickening of the lining of the uterus) and secondary amenorrhea (lack of menstrual cycles) are "off-label" uses, meaning that they do not appear on the FDA-approved labeling. In my experience, obstetricians and other physicians frequently prescribe drugs for off-label uses during pregnancy. Such drugs include tocolytics (*i.e.*, drugs used to delay preterm labor) such as terbutaline, magnesium sulfate, nifedipine, non-steroidal anti-inflammatory drugs (NSAIDs), as well as ampicillin in preterm labor and diabetic medications such as glyburide and metformin for diabetes in pregnancy. In fact, the use of misoprostol for abortion is an off-label use.

14. Several recent studies and a host of older studies have evaluated the use of progesterone to prevent or treat unexplained recurrent miscarriage or early pregnancy bleeding.[8]

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[8] *See, e.g.*, Hassan Shehata et al, *FIGO Good Practice Recommendations on the use of progesterone in the management of recurrent first-trimester miscarriage*, 161 Int'l J. Gynecol. Obstet. 3 (2023) (Exhibit 8); Arri Coomarasamy et al., *Progesterone to prevent miscarriage in women with early pregnancy bleeding: the PRISM RCT*, 24 Health Tech. Assessment, June 2020, at 1 (Exhibit 9); Arri Coomarasamy et al., *Micronized vaginal progesterone to prevent miscarriage: a critical evaluation of randomized evidence*, 223 Am. J. Obstetricians Gynecologists 167, 167-76 (2020) (Exhibit 10); CB Okeke Ogwulu et al., *The cost-effectiveness of progesterone in preventing miscarriages in women with early pregnancy bleeding: an economic evaluation based on the PRISM trial*, 127 BJOG: Int'l J. Obstet. & Gyn. 757 (2020) (Exhibit 11); Arri Coomarasamy et al., *A Randomized Trial of Progesterone in Women with Bleeding in Early Pregnancy*, 380 New Eng. J. Med. 1815 (2019) (Exhibit 12); David M. Haas et al., *Progestogen for preventing miscarriage in women with recurrent miscarriage of unclear etiology*, Cochrane Database of Systematic Revs. (2018) (Exhibit 13); Hayfaa A. Wahabi et al., *Progestogen for*

15. One of the most recent studies, known as the Progesterone in Spontaneous Miscarriage (PRISM) study, examined the use of progesterone in prevention of recurrent miscarriage. The PRISM study followed over 4,000 women at 48 hospitals in the United Kingdom—and found a 3% greater live birth rate among the women who received progesterone therapy. The study concluded that "[p]rogesterone therapy did not result in a significantly higher rate of live births among women with threatened miscarriage *overall*."[9] But it did identify a differential benefit among women with prior miscarriages, showing a 15% greater live birth rate among women with early pregnancy bleeding and three or more prior miscarriages.[10] Arri Coomarasamy, lead author of the PRISM study, stated that "[o]ur research has shown that progesterone is a robust and effective treatment option" that "could prevent 8[,]450 miscarriages a year in the UK."[11]

16. Dr. Cohen misreads these results, selectively claiming that the PRISM study "did not find any statistically significant increase in live births."[12] But she ignores the "increasing live birth rates according to the number of previous miscarriages"

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treating threatened miscarriage, Cochrane Database Systematic Revs. (2018) (Exhibit 14); Hee Joong Lee et al., *The Influence of Oral Dydrogesterone and Vaginal Progesterone on Threatened Abortion: A Systematic Review and Meta-Analysis*, 2017 BioMed Rsch. Int'l, Dec. 17, 2017 (Exhibit 15); Coomarasamy et al., *PROMISE: first-trimester progesterone therapy in women with a history of unexplained recurrent miscarriages*, *supra* note 4, at 1 (Exhibit 5).

[9] *See* Coomarasamy et al., *Progesterone to prevent miscarriage in women with early pregnancy bleeding: the PRISM RCT*, *supra* note 8 (emphasis added).

[10] *Id.*

[11] Jacqui Wise, *NICE recommends progesterone to prevent early miscarriage*, British Med. J. (Nov. 24, 2021) (Exhibit 16).

[12] Cohen Decl. ¶ 16.

among women who received progesterone therapy.[13] As the study authors explained in a follow-up analysis, PRISM in fact shows a "small but positive treatment effect" from progesterone therapy among women with a history of miscarriage.[14] The authors therefore recommended that "the information [about progesterone] should be communicated to women at high risk of miscarriages," concluding that "[w]e believe that a woman at high risk of having a miscarriage may not need absolute scientific certainty to choose to have a treatment. If she is informed about the uncertainty around treatment effects and available safety data, then she could decide for herself the right course of action."[15] Dr. Cohen goes on to quote a 2019 editorial by Dr. Michael Greene that claims the PRISM study as proof that the "enthusiasm" for progesterone therapy to treat threatened miscarriage "was driven by overestimation of the incidence of pregnancy loss in the absence of therapy and *by reports of seeming success in uncontrolled case series*." [16] But as noted above, the authors of PRISM rebutted Greene's view of the study—that the only effects of progesterone are "small" and "sta-

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[13] Coomarasamy et al., *Micronized vaginal progesterone to prevent miscarriage*, *supra* note 8.

[14] *Id.*

[15] *Id.* Dr. Cohen insists that these recommendations "overstate[ ] the results" of the PRISM study by "extrapolating from a small subset of patients with recurrent miscarriage who may benefit from supplemental progesterone to all patients." Cohen Supp. Decl. at 5. But the subset of women with a greater live birth rate following progesterone therapy was not "small"—a total of 1775 women, 1513 women in the PRISM study and 262 in the PROMISE study, gave birth following progesterone therapy. Coomarasamy et al., *Micronized vaginal progesterone to prevent miscarriage, supra* note 8, at Figure 6. Moreover, there is "very good biological reasoning" to expect the PRISM results, given that euploid miscarriages are hypothesized to be caused in part by LPD, and LPD is linked to inadequate progesterone levels. *Id.* at 171.

[16] Cohen Decl. ¶ 16 (emphasis in original) (quoting Michael F. Greene, Editorial, *Progesterone for Threatened Abortion*, 380(19) N. Eng. J. Med. 1867 (2019) (Cohen Decl. Ex. L)).

tistically insignificant"—in a subsequent publication. And the purportedly "uncontrolled case series" cited by Greene is a 1948 study on the use of the estrogen diethylstilbestrol (DES) to prevent complications of pregnancy. DES is a semisynthetic estrogen once used by clinicians to try to reduce the risk of miscarriage in women prone to pregnancy loss, among other reasons. It was pulled from the market after a generation of women who were exposed to it *in utero* developed vaginal cancer. That study does not use progesterone to treat threatened miscarriage.

17. In November 2021, the UK's National Institute of Health and Care Excellence (NICE) published new guidelines recommending progesterone therapy for women with early pregnancy bleeding and at least one previous miscarriage.[17] The recommendation followed a Cochrane review of studies on progesterone use, including the PRISM study. Gillian Leng, NICE's chief executive, stated that "progesterone will not be able to prevent every miscarriage," but "will be of benefit to some women and, as an inexpensive treatment option, can be made available to women on the NHS from today."[18]

18. Importantly, there is no evidence that progesterone poses a safety risk to pregnant women or to their embryos or fetuses. The NICE committee found "no evidence of harms for women or babies" from the use of progesterone, including "no increase

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[17] *Ectopic pregnancy and miscarriage: diagnosis and initial management*, National Institute for Health and Care Excellence (NICE) (updated Nov. 24, 2021) (Guideline NG126, Recommendation 1.5.2) (Exhibit 17).

[18] Wise, *supra* note 11.

in risk of stillbirth, ectopic pregnancy, congenital abnormalities or adverse drug reactions."[19] The American Society for Reproductive Medicine (ASRM) has similarly concluded: "The weight of available evidence indicates that the most common forms of [progesterone] supplementation during early pregnancy pose no significant risk to mother or fetus."[20]

19. Though progesterone has been used in medicine for decades, micronized progesterone received FDA approval in 1998.[21] It is classified as a "Category B" drug for pregnant women—in the same risk category as Tylenol, the most commonly used pain reliever during pregnancy.[22]

B. The abortion pill

20. What is commonly known as the abortion pill refers to the use of prescribed drugs to terminate pregnancy. This procedure is also sometimes known as "medication abortion," "medical abortion," or "chemical abortion."

21. The current abortion-pill regimen uses two drugs, mifepristone (marketed originally as "RU-486" and now as "Mifeprex") and misoprostol. Under the current protocol, a woman takes 200 milligrams of mifepristone orally, followed up to 48 hours later by 800 micrograms of misoprostol buccally (i.e., in the cheek pouch).[23]

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[19] *Ectopic pregnancy and miscarriage: diagnosis and initial management*, National Institute for Health and Care Excellence (NICE) (Nov. 2021) (Guideline NG126 Update) (Exhibit 18).

[20] Prac. Comm. of the Am. Soc. for Reprod. Med., *Progesterone Supplementation During the Luteal Phase and in Early Pregnancy in the Treatment of Infertility: an Educational Bulletin*, 89 Fertility & Sterility 789, 791 (2008) (Exhibit 19).

[21] FDA, Approval Letter (Dec. 16, 1998) (Exhibit 20).

[22] FDA, Prometrium Label at 15 (Exhibit 21); *Prometrium Prescribing Information,* Drugs.com (Exhibit 22).

[23] FDA, Mifeprex Label at 1 (Exhibit 23).

22. Mifepristone is a synthetic steroid developed in the 1980s by a research team led by Etienne-Emile Baulieu at the French pharmaceutical company Roussel-Uclaf.[24] Mifepristone is a progesterone antagonist that works by binding to—and blocking—the progesterone receptors on the nuclear membranes of cells in the uterus and throughout the body.[25] As Baulieu put it, the progesterone receptors are like a keyhole, and mifepristone is the "false key" that fits the lock but cannot open it.[26]

23. By blocking progesterone receptors, mifepristone causes disruption of the developing human embryo's implantation site and suppresses the production of hCG (human chorionic gonadotropin) and progesterone by the placenta. This prevents oxygen and nutrition from being transported to the developing embryo, eventually resulting in the death of the embryo and the embryo's detachment from the endometrium.[27] Mifepristone also softens the cervix and increases the sensitivity of the uterus to agents that cause uterine contractions.[28]

24. As Dr. Cohen correctly acknowledges, mifepristone alone is not always effective in ending a pregnancy.[29] Misoprostol is included in the abortion pill regimen to

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[24] *See generally The Antiprogestin Steroid RU 486 and Human Fertility Control* (Etienne-Emile Baulieu & Sheldon J. Segal eds., 1985) (Exhibit 24).

[25] *See id.* at 276 ("Our results confirm that RU 486 behaves as a progesterone antagonist at the receptor level.").

[26] Cristine Russell, *Chemical Found by French Could Lead to Monthly Birth Control Pill*, Washington Post (Apr. 20, 1982) (Exhibit 25).

[27] Marja-Liisa Swahn & Marc Bygdeman, The effect of the anti-progestin RU486 on uterine contractility and sensitivity to prostaglandin and oxytocin, 95 BJOG: Int'l J. Obstet. & Gyn. 126-134, Feb. 1988 (Exhibit 26).

[28] Mary L. Davenport et al., *Embryo Survival After Mifepristone: A Systematic Review of the Literature*, 32 Issues L. & Med. 3 (2017) (Exhibit 27).

[29] Cohen Decl. ¶ 9.

improve its overall efficacy rate and achieve complete expulsion of the embryo. Misoprostol works by binding to smooth muscle cells in the uterine lining, causing contractions that mechanically expel the embryo, placenta, and membranes from the uterus.

25. According to a scoping review (DeBeasi) published in July 2023, the continuing pregnancy rate for women who take mifepristone alone is generally 25% or less at gestational ages of 49 days or less.[30] This result is consistent with a 2017 paper (Davenport) that analyzed data from early mifepristone studies and concluded that the continuing pregnancy rate after mifepristone alone was up to 23%.[31]

26. Dr. Cohen's response to the DeBeasi study is to complain that the journal that published it is a publication of the Catholic Medical Association, and "not a journal that is typically utilized by OB/GYNs for dissemination of clinically relevant data."[32] But whether a journal is devoted to the "dissemination" of OB-GYN clinical data is irrelevant to the strength or accuracy of a particular study. Indeed, numerous other non-OB-GYN journals—including *PLOS One*, for which Dr. Cohen serves as a reviewer[33]—can and do publish articles of interest to OB-GYNs.

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[30] Paul L.C. DeBeasi, *Mifepristone Antagonization with Progesterone to Avert Medication Abortion: A Scoping Review*, The Linacre Quarterly (July 2023) (Exhibit 28).

[31] Davenport et al., *supra* note 28; *see also* Mitchell Creinin et al., *Mifepristone Antagonization with Progesterone to Prevent Medical Abortion: A Randomized Controlled Trial*, 135(1) Obstetrics & Gynecology 158 (2020) (Exhibit 29) (estimating that "only 25%" of patients receiving mifepristone and placebo would have continuing pregnancies).

[32] Cohen Decl. ¶ 31.

[33] *Id.* ¶ 3.

27. Dr. Cohen goes on to denigrate the credentials of the study author, Paul DeBeasi, complaining that he is "not a physician" and that he graduated from "a small Catholic university."[34] It is worth noting that Mr. DeBeasi is the former chief of research for Gartner, one of the most prestigious research organizations not just in the country, but in the world. And as Dr. Cohen also admits, "[t]he purpose of a scoping review is to *synthesize evidence*"—and she offers no critique of either the review's data analysis (which is sound) or its conclusion confirming the 25% or less continuing pregnancy rate for women who take mifepristone alone.[35] Instead, she cites a statistic that appears to be irrelevant to a discussion of Mr. DeBeasi's paper, from an article on outcomes following medication abortion.[36]

28. Dr. Cohen's claim that "as many as 46%" of women who take mifepristone without misoprostol will continue their pregnancies is not supported by solid data.[37] The 46% figure rests on a single study with important flaws (Zheng) that defined "persisting pregnancy" as "no expulsion of the conceptus" and "gradual" increase of serum or urine hCG.[38] The Zheng study did not use ultrasound to verify the presence of a living embryo or fetus—and thus failed to distinguish between a continuing preg-

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[34] *Id.* ¶ 31.

[35] *Id.* at ¶ 32 (emphasis added).

[36] *Id.* (citing Kelly Cleland et al., *Significant Adverse Events and Outcomes After Medical Abortion*, 121(1) Obstetrics & Gynecology 166-71 (2013) (Cohen Decl. Ex. P)).

[37] Cohen Decl. ¶ 9 (citing Zheng Shu-rang, *RU 486 (Mifepristone): Clinical Trials in China*, 149 Acta Obstetricia Gynecologica Scand. Suppl. 19, 21 (1989) (Cohen Decl. Ex. E)).

[38] Zheng Shu-rang, *RU 486 (Mifepristone): Clinical Trials in China*, 149 Acta Obstetricia Gynecologica Scand. Suppl. 19, 21 (1989) (Cohen Decl. Ex. E).

nancy (i.e., a living embryo or fetus), retained fetal and placental parts (i.e., an incomplete abortion), or ectopic pregnancy.[39] The 2017 Davenport paper carefully analyzed data from early mifepristone studies and concluded that the Zheng study was "not reliable for determining the rate of embryo survival."[40]

C. Abortion pill reversal

29. When a woman has taken mifepristone and then decides that she wishes to continue her pregnancy, it no longer makes sense for her to take misoprostol. The first step in halting the abortion pill process is for the patient not to take misoprostol.

30. Health care providers may then seek to help the woman by prescribing progesterone in an attempt to overcome the fetotoxic effects of mifepristone and keep the embryo or fetus alive. Administering progesterone in these circumstances is commonly known as "abortion pill reversal."

31. Dr. Cohen opines at length about the importance of decisional certainty, claiming that it is "exceedingly rare" for women to change their mind about abortion, and that "somewhere between 0.005% and .3% of patients change their mind after taking mifepristone."[41] But the policy guideline paper she cites for that statistic—by Alice Mark of the National Abortion Federation—states that "[i]n most clinical trials

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[39] DeBeasi, *supra* note 30.

[40] *See, e.g.*, Davenport et al., *supra* note 28; *cf.* Creinin et al., *supra* note 31 (estimating that "only 25%" of patients receiving mifepristone and placebo would have continuing pregnancies).

[41] Cohen Decl. ¶ 11; *see also id.* ¶ 40 ("the data suggests far fewer than 1% of women elect to continue their pregnancies after taking mifepristone").

of early medication abortion, *the number of subjects taking mifepristone without misoprostol is not reported*."[42] In other words, the statistic Dr. Cohen touts for the proposition that "patients … rarely change their minds after taking mifepristone" derives from a policy guideline document disclosing that such data are not reported in most clinical trials.[43]

32. Like most other uses of supplemental progesterone, the use of progesterone for abortion pill reversal is an "off-label" use.

33. The basic biochemical premise of abortion pill reversal is that the activity of a receptor antagonist can be inhibited by increasing the concentration of the receptor agonist.[44] Put differently, it is well established that the effect of competitive inhibitors (*e.g.*, mifepristone) that block substrates (*e.g.*, progesterone) can be thwarted by

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[42] Alice Mark et al., *When Patients Change Their Minds After Starting an Abortion: Guidance from the National Abortion Federation's Clinical Policies Committee*, Contraception 101(5):283-285 (2020) (Cohen Decl. Ex. I) (emphasis added).

[43] Cohen Decl. at 5. Dr. Cohen further relies on the rigor of her own initial consultation with abortion patients, stating that she "ensure[s] they are not under duress, being coerced into obtaining an abortion, or uncertain about their decision," and that she "take[s] a detailed history from the patient," "screen[s] for risk factors for domestic violence," and "separate[s] the patient" from any family members or intimate partners present "to make sure they are not being coerced or under threat of harm." *Id.* ¶ 12. But even assuming all that is true, Dr. Cohen does not—and cannot—testify that comparable practices are followed in every clinic in Colorado. More importantly, Dr. Cohen fails to acknowledge that the FDA's 2016 REMS for mifepristone "[r]emov[ed] … the instruction that administration of misoprostol must be done in-clinic," *i.e.*, in person with a physician. FDA Summary Review of 2016 Amendments at 2 (Mar. 29, 2016) (Exhibit 30). It is simply not possible to follow the screening mechanisms Dr. Cohen identifies when the doctor-patient relationship is limited to a single telehealth appointment.

[44] *See generally* Barbara J. Pleuvry, *Receptors, agonists and antagonists*, 5 Neurosurgical Anaesthesia and Intensive Care, Pharmacology 350 (2004) (Exhibit 31).

adding more substrate.[45] Abortion pill reversal—which involves administering a surplus of progesterone to outcompete mifepristone binding and block its effects—is modeled on these basic principles of biochemistry.

34. Counteracting the effects of a receptor antagonist by introducing higher doses of the receptor agonist is not a new idea. One widely used example from emergency medicine is treatment of carbon monoxide poisoning. In normal respiration, oxygen in the lungs binds to the hemoglobin molecule in red blood cells in the lungs, and then is carried to tissues throughout the body. Carbon monoxide causes hypoxia (low oxygen) because it binds more tightly to hemoglobin than oxygen—its affinity for hemoglobin is more than 200 times that of oxygen.[46] But when a patient with carbon monoxide poisoning arrives in the emergency room, she is quickly treated with high-flow oxygen therapy. That is because, even though carbon monoxide binds more tightly to hemoglobin than oxygen, carbon monoxide binding to the hemoglobin molecule is reversible. In other words, oxygen can effectively compete with, and outcompete, carbon monoxide for hemoglobin binding sites.

35. Dr. Cohen states that "there is no reliable scientific evidence supporting the use of exogenous progesterone to break mifepristone's bind to the progesterone receptors."[47] This statement is false. Below are some of the studies, from both the basic science and clinical literature, showing that progesterone can effectively compete with and outcompete mifepristone for progesterone binding sites.

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[45] *See* John W. Pelley, *Elsevier's Integrated Review Biochemistry* (2d ed. 2011) 33-34 (Exhibit 32).

[46] Lindell K. Weaver, *Carbon Monoxide Poisoning*, 360(12) New Eng. J. Med. (2009) (Exhibit 33).

[47] Cohen Decl. ¶ 17.

36. Animal studies indicate that administering additional progesterone can counteract the effects of mifepristone. In 1989, researchers designed a study (Yamabe) to investigate "the role of progesterone in the maintenance of pregnancy" using a population of pregnant rats.[48] After four days, only 33.3% of the rats who received mifepristone remained pregnant—but 100% of the rats who were given progesterone simultaneously with mifepristone remained pregnant. The Yamabe study therefore indicates that progesterone can counteract mifepristone's binding to progesterone receptors.

37. Another animal study (Camilleri & Sammut) published in July 2023 supports that same conclusion. Researchers designed a follow-on to the Yamabe study to evaluate the "non-simultaneous, subsequent administration" of progesterone following mifepristone in a population of pregnant rats.[49] No rats who received mifepristone alone at first-trimester human gestational age equivalent (approximately 4-6 weeks' human gestation) remained pregnant, while 81.3% of rats who received mifepristone followed by progesterone at the same stage remained pregnant. The study concludes that "[t]he administration and actions of the natural agonist, progesterone, in the presence of the antagonist, mifepristone, appears to be in concordance with the liter-

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[48] Shingo Yamabe et al., *The Effect of RU486 and Progesterone on Luteal Function During Pregnancy*, 65 Folia Endocrinologica Japonica 497 (1989) (Exhibit 34).

[49] Christina Camilleri & Stephen Sammut, *Progesterone-mediated reversal of mifepristone-induced pregnancy termination in a rat model: an exploratory investigation*, 13 Scientific Reports 10942 (2023) (Exhibit 35).

ature and our understanding of the pharmacological functioning of reversible competitive antagonism, where sufficient levels of the agonist can override a given concentration of an antagonist."[50]

38. In 2012, Dr. George Delgado and Dr. Mary Davenport published a small case series that followed seven women who had taken mifepristone and then received progesterone therapy after seeking medical assistance to maintain their pregnancies.[51] Four of the six women (66%) who completed the study carried their pregnancies to term and delivered live infants. No birth defects were observed.

39. A similar small case series out of Australia (Garratt & Turner) was published in the *European Journal of Contraceptive and Reproductive Health Care* in 2017.[52] In that series, two out of three women (66%) who received progesterone therapy after ingesting mifepristone carried their pregnancies to term and delivered healthy live infants.

40. In 2018, Dr. George Delgado and his co-authors published a larger case series that followed 754 pregnant women who had taken mifepristone, but had not yet taken misoprostol, and were interested in reversing its effects. The 2018 study analyzed the charts of 547 women who had ingested mifepristone within the last 72 hours and then

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[50] *Id.*

[51] George Delgado & Mary L. Davenport, *Progesterone use to reverse the effects of mifepristone*, 46 Annals of Pharmacotherapy 1723 (2012) (Exhibit 36).

[52] Deborah Garratt & Joseph V. Turner, *Progesterone for preventing pregnancy termination after initiation of medical abortion with mifepristone*, 22 Eur. J. Contraceptive & Reprod. Health Care 472 (2017) (Exhibit 37).

received progesterone therapy.[53] The study found an overall fetal survival rate of 48%.[54]

41. The 2018 Delgado study showed even higher survival rates when the patients were divided into treatment subgroups. The subgroup that received progesterone intramuscularly showed fetal survival rates of 64%, and the subgroup that received a high dose of oral progesterone followed by daily oral progesterone until the end of the first trimester had survival rates of 68%.[55]

42. The 2018 Delgado study used data from a previous study as a historical control to determine how these fetal survival rates compared to those of women who took mifepristone alone. That data was derived from a systematic review, published by Dr. Davenport in 2017, that surveyed the existing literature on outcomes for women who had taken mifepristone but not misoprostol and found fetal survival rates that ranged from 10% to 23.3%.[56] In the 2018 study, Dr. Delgado and his co-authors chose to use a number for historical controls (25% survival) that was higher than Dr. Davenport's highest number (23.3% survival). Even so, the fetal survival rates for women who received progesterone therapy—48% up to 68%—compare favorably to the baseline number.

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[53] George Delgado et al., *A Case Series Detailing the Successful Reversal of the Effects of Mifepristone Using Progesterone*, 33 Issues L. & Med. 21, 25-26 (2018) (Exhibit 38).

[54] *Id.* at 26-27.

[55] *Id.* at 26-27.

[56] Davenport et al., *supra* note 28.

43. Notably, the 2018 Delgado study found no increased risk of birth defects after progesterone therapy following mifepristone administration. This result is consistent with other studies that have found no increased incidence in birth defects in infants born after exposure to mifepristone in the first trimester.[57] The 2018 Delgado study also found that the rate of preterm delivery among women who received progesterone therapy was 2.7%, compared with a 10% average in the general population in the United States.[58]

44. Even before the 2018 Delgado study was published, Dr. Harvey Kliman, the director of the reproductive and placental research unit at the Yale School of Medicine, told the *New York Times* that using progesterone to reverse the effects of mifepristone "makes biological sense" and is "totally feasible."[59] Dr. Kliman further stated that "if one of his daughters came to him and said she had somehow accidentally taken mifepristone during pregnancy … he would tell her to take 200 milligrams of progesterone three times a day for several days, just long enough for the mifepristone to leave her system: 'I bet you it would work.'"[60]

45. Even more telling is the 2020 ACOG joint practice bulletin. As discussed below, *infra* at ¶ 64, Dr. Cohen cites the joint bulletin in support of her claim that "there

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[57] *See, e.g.*, FDA, Mifeprex Label at 9, *supra* note 23 (noting that no teratogenic effects have been noted in experiments with rats and mice); *see also* N. Bernard et al., *Continuation of pregnancy after first-trimester exposure to mifepristone: an observational prospective study*, BJOG: Int'l J. Obstet. & Gyn. 568 (2013) (Exhibit 39).

[58] Delgado et al., *supra* note 53.

[59] Ruth Graham, *A New Front in the War Over Reproductive Rights: 'Abortion-Pill Reversal'*, N.Y. Times, July 18, 2017 (Exhibit 40).

[60] *Id.*

is no evidence suggesting that using progesterone after taking mifepristone increases the likelihood of a pregnancy continuing."[61] But that same bulletin also warns that "[p]atients who select depot medroxyprogesterone acetate (DMPA)"—a synthetic progesterone-like steroid—"for contraception should be counseled that administration of DMPA on day 1 of the medication abortion regimen *may increase the risk of ongoing pregnancy*."[62] It goes on to state:

> Concern has been raised that the immediate use of hormonal contraception that contains progestins could theoretically interfere with medication abortion efficacy … DMPA injection at the time of mifepristone administration may slightly increase the risk of an ongoing pregnancy. In a randomized trial that evaluated the effects of DMPA injection timing on medication abortion outcomes, ongoing pregnancy was more common among those randomized to receive DMPA injection on the day of mifepristone administration compared with those who received DMPA at a follow-up visit (3.6% versus 0.9%; 90% CI, 2.7 [0.4–5.6]).[63]

Thus, ACOG itself warns patients that using a progestin—a synthetic progesterone-like compound—on the same day as mifepristone decreases the effectiveness of mifepristone and "increase[s] the risk of ongoing pregnancy." That warning is consistent with the overall body of scientific evidence that supports abortion pill reversal.

46. Finally, the same study cited by Dr. Cohen—and ACOG, and the National Abortion Federation, and many others—in support of alleged safety concerns about

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[61] Cohen Decl. ¶ 35 (citing Am. Coll. of Obstetricians & Gynecologists, *Practice Bulletin No. 225*: *Medication Abortion up to 70 Days of Gestation*, 136 Obstetrics & Gynecology 1, 3 (2020) (Cohen Decl. Ex. S)).

[62] Am. Coll. of Obstetricians & Gynecologists, *Practice Bulletin No. 225*: *Medication Abortion up to 70 Days of Gestation*, 136 Obstetrics & Gynecology 1, 8 (2020) (emphasis added) (Cohen Decl. Ex. S).

[63] *Id.* at 8-9.

abortion pill reversal in fact shows progesterone's effectiveness in reversing the effects of mifepristone. As discussed below, *infra* at ¶¶ 65-67, Dr. Mitchell Creinin attempted to conduct a randomized study on the "efficacy and safety" of abortion pill reversal.[64] The study was designed to enroll 40 pregnant women in two control groups—one receiving mifepristone followed by progesterone, and the other receiving mifepristone followed by a placebo. But the study was halted after 12 women were enrolled, and only 10 women completed it. Notably, four of the five women (80%) in the progesterone group of the Creinin study successfully maintained their pregnancies, as documented by fetal cardiac activity. In contrast, only two of the women in the placebo group (40%) maintained their pregnancies. These results are also consistent with the overall body of scientific evidence that supports abortion pill reversal.

D. Dr. Cohen's summary of the scientific evidence is selective and inaccurate

47. In the declaration she previously submitted in this case, Dr. Rebecca Cohen opines that "there is no scientific support for so-called 'medication abortion reversal.'"[65] But she bases this erroneous conclusion on an incomplete review of the relevant literature and a selective and inaccurate summary of the scientific evidence.

48. Notably, Dr. Cohen does not dispute the results of the animal studies indicating that progesterone can counteract the effects of mifepristone, or the Australian

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[64] Creinin et al., *supra* note 31.

[65] Cohen Decl. at 8 (cleaned up).

case series, or the efficacy results of the Creinin study.[66] Nor does she dispute the ACOG Practice Bulletin warning that use of a progestin on the same day as mifepristone "increase[s] the risk of ongoing pregnancy," *supra* at ¶ 45—in fact, she explicitly concedes that these results may demonstrate the "*biological plausibility*" of abortion pill reversal.[67] As noted above at ¶¶ 16-17, Dr. Cohen's attempt to downplay the effects of progesterone in the PRISM study is undermined by a misreading of the study's relevant results and is rebutted by the PRISM authors themselves.

49. Instead, Dr. Cohen focuses her attention and criticisms on the two studies by Dr. George Delgado. These critiques—many of which are flawed or overstated or both—fail to show that there is "no scientific support" for abortion pill reversal.[68]

50. To begin, many of Dr. Cohen's critiques boil down to the fact that Dr. Delgado's studies are case series rather than randomized controlled trials. In a randomized controlled trial, study participants are carefully selected to minimize differences between patient groups. They are then randomly assigned either to a treatment group or a control group. The treatment group receives the treatment at issue, and the control group receives either a placebo or standard treatment. By contrast, a case series involves a collection of reports on the treatment of individual patients with the same

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[66] In a supplemental declaration, Dr. Cohen opines that "[a]nimal studies cannot establish safety or efficacy of a treatment in humans." Cohen Supp. Decl. at 2. But she does not contest that animal studies "can provide important foundational information about drug mechanisms, toxicity, and effectiveness." *Id.* at 1. Animal studies are only a single component of the scientific evidence that supports abortion pill reversal. *See supra* at ¶ 7.

[67] Cohen Supp. Decl. at 3 (emphasis added).

[68] *Id.* at 8; *id.* ¶¶ 15, 18-30.

condition. A randomized controlled trial is generally considered the "gold standard" in medical research.

51. In some clinical situations, case series and observational studies are the only appropriate source of data, since randomizing one group of patients to a placebo would be unethical. For example, it would be unethical to use a placebo arm in a study of cancer therapy where effective treatment exists. Likewise, it would be unethical to use a placebo arm in a study of abortion pill reversal where women have ingested mifepristone but then changed their minds and decided to carry their babies to term.

52. Physicians can and do use the results of case series to integrate innovative therapeutic treatments into their practices. Case series are commonly used in studies involving pregnant women. Many drugs used in obstetrics and gynecology came into clinical usage based on data from case series alone. These include magnesium sulfate for prevention of preterm labor and eclampsia (seizures due to high blood pressure in pregnancy); terbutaline for prevention of preterm birth; nifedipine for prevention of preterm birth; hydralazine for control of hypertension in pregnancy; and methotrexate for treatment of ectopic pregnancy, among others. Notably, mifepristone itself was approved by the FDA based on non-blinded, non-randomized studies.[69] None of the studies used for mifepristone's approval were randomized controlled trials.

[69] Irving M. Spitz et al., *Early Pregnancy Termination with Mifepristone and Misoprostol in the United States*, 338(18) N. Eng. J. Med. 1241 (1998) (Exhibit 41).

53. Dr. Cohen critiques the 2012 Delgado study because "[a] six-person sample size is far too small to draw any statistically significant generalizations."[70] But the 2012 Delgado study, like most case series, does not present any statistical analyses.

54. Dr. Cohen further claims that the 2018 Delgado study failed to "adhere[] to any ethical and regulatory standards of clinical trials," failed to "use a concurrent control group," and failed to use a single progesterone regimen.[71] But the 2018 Delgado study was not a clinical trial, nor was it presented as such. Rather, the study makes clear that its analysis is based on data collected from the abortion pill reversal hotline: "Subjects called an informational hotline linked to an informational website and staffed by nurses and a physician assistant. After receiving information about the reversal process, those who decided to proceed with reversal were referred to physicians and mid-level practitioners in their respective geographic areas for treatment."[72] The study did not use a concurrent control group because it was not a case-control study, and because the use of a placebo control group would be unethical in this scenario. And because the authors were collecting real-world data on different protocols in use, it is not surprising that different regimens were included.

55. Dr. Cohen further states that Dr. Delgado and his co-authors originally labeled the 2018 study an "observational case study," which she claims—without citation—is "not a study design generally used in medical research."[73] This is not true.

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[70] Cohen Decl. ¶ 19.

[71] *See, e.g.*, *id.* ¶¶ 20, 25, 29-30.

[72] Delgado et al., *supra* note 53.

[73] Cohen Decl. ¶ 24.

The term "observational case study" is a legitimate study design documented in the medical literature.[74]

56. Dr. Cohen further alleges "selection bias" because patients were included in the Delgado studies after an ultrasound screening confirmed a living embryo prior to the first progesterone dose.[75] But the purpose of the studies was to evaluate the use of progesterone in reversing the effects of mifepristone and continuing the pregnancy. It would be irrational to administer progesterone to a woman whose embryo was already dead or to include those patients in the analysis.

57. Dr. Cohen also criticizes the Institutional Review Board (IRB) approval of the 2018 Delgado study.[76] But the final version of the 2018 Delgado study clearly states that "[t]he study was reviewed and approved by an institutional review board."[77]

58. I disagree with Dr. Cohen's statement that the 2018 Delgado study "violated several ethical standards of medical research."[78] She does not state what standards she is referring to or how they were violated. Based on my experience as a reviewer and IRB member over more than a decade, I see no ethical violations in this research, which is a straightforward observational case series.

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[74] *See, e.g.*, Sonya J. Morgan et al., *Case Study Observational Research: A Framework for Conducting Case Study Research Where Observation Data Are the Focus*, 27 Qualitative Health Rsch. 1060, 1060-1068 (2017) (Exhibit 42); Assad A Rezigalla, *Observational Study Designs: Synopsis for Selecting an Appropriate Study Design*, 12 Cureus (2020) (Exhibit 43); Julia FM Gilmartin-Thomas et al., *Observational studies and their utility for practice,* 41 Australian Prescriber 82 (2018) (Exhibit 44).

[75] Cohen Decl. ¶¶ 21, 30.

[76] *Id.* ¶ 26.

[77] Delgado et al., *supra* note 53.

[78] Cohen Decl. ¶ 28.

59. After criticizing the Delgado studies—and ignoring the balance of the scientific evidence—Dr. Cohen proceeds to cite two studies by Dr. Daniel Grossman for the proposition that "[s]cientifically valid research finds insufficient data to support progesterone therapy over expectant management."[79] Neither of the cited studies supports this conclusion.

60. To begin, Dr. Grossman's 2015 literature review concluded that the "evidence is insufficient to determine whether treatment with progesterone after mifepristone results in a higher proportion of continuing pregnancies compared to expectant management."[80] But that conclusion was based solely on an analysis of the 2012 Delgado study, which of course predates the 2017 Australian study, the 2018 Delgado study, the 2020 PRISM study, the 2020 Creinin study, the 2023 DeBiasi study, and the 2023 Camilleri & Sammut study.

61. Moreover, Dr. Grossman's conclusion—that there was insufficient evidence to show that progesterone therapy improved fetal survival—was based on the reportedly high continuing pregnancy rates from a series of studies in the 1980s. Based on these studies, Dr. Grossman claimed that the continuing pregnancy rate for women who take mifepristone alone is up to 46%.[81] But Dr. Grossman's "systematic review" of 11 studies included four studies—among them the Zheng study discussed *supra* at

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[79] *Id.* at 16.

[80] Daniel Grossman et al., *Continuing Pregnancy after Mifepristone and "Reversal" of First-Trimester Medical Abortion: A Systematic Review*, 92(3) Contraception 206 (2015) (Cohen Decl. Ex. Q).

[81] *Id.* at 208.

¶ 29—that failed to distinguish between continuing pregnancy and retained "products of conception" (*i.e.*, an incomplete abortion)."[82] In other words, four of the 11 studies included in Dr. Grossman's literature review estimated embryo survival rates without using an ultrasound to verify the presence of a living embryo. Further, Dr. Grossman failed to include five more studies that *did* report on whether there was a live embryo after the use of mifepristone.[83] These methodological flaws seriously undermine both Dr. Grossman's estimates of continuing pregnancy rate and his evaluation of the efficacy of progesterone therapy relative to expectant management following mifepristone.[84]

62. Dr. Cohen then states that "Dr. Grossman published a second article, this time in the *New England Journal of Medicine*."[85] She fails to note that this was published in the "Perspective" section of the journal—and is therefore clinical commentary or opinion, not a research study. In the article, Dr. Grossman criticizes various aspects of the 2018 Delgado study. He goes on to claim that "a randomized, placebo-controlled trial is the most appropriate study design" for research on abortion pill

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[82] DeBeasi, *supra* note 30.

[83] Davenport et al., *supra* note 28.

[84] Dr. Cohen touts *Contraception*, the journal in which the 2015 Grossman review was published, as a "highly cited journal regularly relied upon by OB/GYNs and clinicians in the reproductive health field." Cohen Decl. ¶ 33. She fails to mention that it is the official journal of the Society of Family Planning, which is openly committed to a "vision of just and equitable abortion" and has signed onto numerous amicus briefs in court cases concerning abortion access. Society of Family Planning, *Diversity, Equity, and Inclusion* (Exhibit 45). Nor does she mention that Dr. Grossman has served as a paid advisor to Planned Parenthood. Daniel Grossman ICMJE Form for Disclosure of Potential Conflicts of Interest, May 23, 2018, at 2-3 (Exhibit 46).

[85] Cohen Decl. ¶ 34 (citing Daniel Grossman & Kari White, *Abortion "Reversal"—Legislating Without Evidence*, 379(16) N. Eng. J. Med. 1401 (2018) (Cohen Decl. Ex. R)).

reversal—with no apparent concern for the ethical problems posed by assigning women who wish to continue their pregnancies to a placebo group.[86]

63. Dr. Cohen cites a joint practice bulletin from ACOG and the Society of Family Planning and the National Abortion Federation clinical policy guidelines as further support for her opinions.[87] Both publications claim that there is "no evidence" that using progesterone after taking mifepristone increases the likelihood of a continuing pregnancy.[88] But both rely exclusively on Grossman's 2015 study (critiqued above at ¶¶ 61-62) and Creinin's 2020 study (discussed below at ¶¶ 65-67) and address none of the other relevant literature.

64. Dr. Cohen next claims that the *other* off-label uses of progesterone "that meet generally accepted standards of medical practice have been subjected to the research, data collection, analysis, and reporting in journals commonly relied upon by practitioners."[89] But she does not identify which of the many off-label uses are "generally accepted" in her view and which are not. The only example she offers is "the study [that] … specifically explored the efficacy of progesterone for patients with threatened miscarriages in the first trimester"—an apparent reference to PRISM, the same study she previously misread as finding no statistical significance for progesterone therapy

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86 Grossman, *supra* note 85.

87 Cohen Decl. ¶ 35.

88 Am. Coll. of Obstetricians & Gynecologists, Practice Bulletin No. 225, *Medication Abortion up to 70 Days of Gestation*, 136 Obstetrics & Gynecology 1, 3 (2020) (Cohen Decl. Ex. S); 5 Nat'l Abortion Fed'n, Clinical Policy Guidelines for Abortion Care 18 (2020) (Cohen Decl. Ex. T).

89 Cohen Decl. ¶ 36.

in patients with threatened miscarriage.[90] Moreover, Dr. Cohen is wrong to suggest that all other off-label uses for progesterone were subjected to randomized controlled trials prior to widespread use within obstetrics. For example, OB-GYNs began using progesterone in the 1940s, long before any clinical trials were conducted. The assertion that off-label drugs can only be legitimately used after clinical trials have been performed is false. Finally, Dr. Cohen claims that a 2020 study by Dr. Mitchell Creinin raised "significant safety concerns."[91] Dr. Creinin attempted to conduct a randomized study on the "efficacy and safety" of abortion pill reversal. The study was designed to enroll 40 pregnant women in two control groups—one receiving mifepristone followed by progesterone, and the other receiving mifepristone followed by a placebo. But Dr. Creinin stopped the study after 12 women were enrolled, and only 10 women completed it.

65. Dr. Cohen obliquely claims that the Creinin study was halted "because three participants experienced severe hemorrhage that required emergency medical care."[92] But two of those women were in the placebo group, so the only drug they had received was mifepristone. Those women required emergency curettage/suction procedures to control bleeding, and one of them required a blood transfusion. But for the

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[90] *Id.* ¶ 36 (referring to "the study described in paragraph 15 above"); *see id.* ¶ 16.

[91] Cohen Decl. ¶ 37 (citing Creinin et al., *supra* note 31).

[92] Cohen Decl. ¶ 38.

one woman who had received progesterone and had significant bleeding, no intervention was required.[93] Nowhere in the study does Dr. Creinin contend that progesterone itself is the danger, focusing instead on the purported danger of not taking misoprostol.

66. In addition, four of the five women (80%) in the progesterone group of the Creinin study successfully maintained their pregnancies, as documented by fetal cardiac activity. In contrast, only two of the women in the placebo group (40%) maintained their pregnancies. These results directly undermine her conclusion that progesterone therapy is "no more effective than watchful waiting."[94]

67. In summary, there is scientific evidence that supports the clinical use of progesterone to counteract the effects of mifepristone. Progesterone in a variety of formulations has well established clinical uses and an extensive, decades-long track record of safety and is used off label for several clinical purposes. Multiple studies over time have evaluated the use of progesterone to prevent or treat unexplained recurrent miscarriage or early pregnancy bleeding. Research indicates that the continuing pregnancy rate after mifepristone alone for abortion is 23-25%. There is evidence that abortion pill reversal is a safe and effective option for women who change their minds after ingesting mifepristone for abortion. Abortion pill reversal is based on sound basic science and biochemistry, and evidence suggests that it is safe and reduces the risk of completed induced abortion after mifepristone alone. Importantly, evidence

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93 Creinin et al., *supra* note 31 ("Heavy bleeding lasted about 3 hours overall, and no intervention was needed.").

94 Cohen Decl. ¶ 40.

also suggests that abortion pill reversal is a compassionate, safe, and effective response to support a woman's reproductive autonomy as well as her desire to keep her child.[95]

68. Based on the foregoing, I conclude that there is scientific evidence to support the use of progesterone to reverse the effects of mifepristone and help women who desire to carry their children to term.

[NOTHING FURTHER ON THIS PAGE]

[95] Katherine A. Rafferty & Tessa Longbons, *Understanding Women's Communications with Their Providers During Medication Abortion and Abortion Pill Reversal: An Exploratory Analysis*, 90 The Linacre Quarterly 172 (2023) (Exhibit 47).

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Executed on this 31st day of May, 2024.

Monique Chireau Wubbenhorst

Monique Chireau Wubbenhorst