EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF NEW YORK

NATIONAL INSTITUTE OF FAMILY AND LIFE ADVOCATES, GIANNA'S HOUSE, INC., and CHOOSE LIFE OF JAMESTOWN, INC. d/b/a OPTIONS CARE CENTER, *Plaintiffs*, v. LETITIA JAMES, in her official capacity as Attorney General of the State of New York, *Defendant*.	Case No.: 1:24-cv-00514

EXPERT DECLARATION OF CHRISTINA FRANCIS, M.D.

I, Christina Francis, M.D., pursuant to 28 U.S.C. section 1746, do hereby declare as follows:

1. I am at least 18 years of age and am competent to testify. I have personal knowledge of the statements contained in this declaration. The opinions expressed in this report are my own and do not represent the views of any organization with which I am associated.

I. Background and Qualifications

2. I have been a practicing obstetrician and gynecologist for fifteen years, board-certified for twelve years, and currently practice in Fort Wayne, Indiana. I work as an OB/GYN Hospitalist, which entails caring for pregnant women and their babies ranging from routine to high-risk pregnancies in the inpatient setting, as well as managing inpatient gynecological consults and emergencies. I am also CEO of the American Association of Pro-Life Obstetricians and Gynecologists (AAPLOG), a national professional organization of more than 7,000 pro-life medical practitioners.

3. I graduated from medical school at Indiana University in 2005 and completed my obstetrician and gynecologist residency at St. Vincent Hospital in Indianapolis in 2009.

4. 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.

II. Expert Opinions and Bases for Them

5. I have reviewed the statements on Plaintiffs' websites concerning the safety and efficacy of abortion pill reversal/rescue (APR), and it is my professional opinion that they are accurate and non-misleading.

6. NY Attorney General James states in her filing (paragraph 120) that the APR network website states that the APR protocol is effective after 72 hours. This is false. The website states that it may not be too late even if it's been more than 72 hours since a woman has taken mifepristone and that she can still call. It is possible that the embryo or fetus could still be living and in that case it would not be too late. They make no claims of efficacy after that point on their website. However, if a woman wants to save her baby she should call. They can get her connected to ultrasound. If her baby is still alive, progesterone would not be contraindicated. It is used for early pregnancy support by Reproductive Endocrinology and Infertility (REI) specialists quite frequently for pregnancy support in the first trimester.

A. My APR Practice.

7. I have been providing APR through the Abortion Pill Rescue Network since 2015. The APR network is a network of medical practitioners who are readily available to administer the APR protocol to women who regret their abortion decision and desire to save their preborn child. Women are connected to those practitioners through the network hotline, which is manned 24/7 by a trained nurse.

8. In the fall of 2015, I assisted a patient who began an abortion at a Planned Parenthood clinic and then immediately regretted her decision. She knew the very minute she left the clinic that she made the wrong choice. She found out about APR by Google web search. The patient was connected to me through the APR hotline. By administering progesterone according to the APR protocol (explained in more detail below), that patient was able to successfully continue her pregnancy and delivered a healthy baby with no medical issues in 2016.

9. Since then, I have spoken with more women who called the network and chose to start APR and with some who haven't. No woman is ever pressured to start the progesterone protocol but rather is counseled on her options and the risks and benefits of each of those options. She is then provided support through her decision. AG James' claim in paragraph 125 that Heartbeat International's statements that APR increases the chances of a woman's pregnancy continuing "are likely to mislead a consumer considering APR treatment because they address an issue that is at the heart of that consumer's decision-making—will APR increase the likelihood that my pregnancy will continue?" is nonsensical. Every consumer considers prior to taking a medication whether what it is for is something they desire or need and whether it is going to be effective.

10. Since my first successful chemical abortion rescue, I have helped other women save their children's lives by taking progesterone after they regretted taking mifepristone.

B. Chemical Abortions and How They Can Be Reversed.

11. Chemical abortions typically involve a two-drug regimen: mifepristone followed by misoprostol. Mifepristone is a progesterone receptor antagonist, which inhibits the effect of progesterone, a crucial hormone for normal fetal development. Progesterone is essential to achieve and maintain a healthy pregnancy. It prepares the uterine lining to allow implantation and stimulates glands in the lining to secrete

nutrients for the early embryo. During the first 8 weeks of pregnancy, progesterone is produced by the corpus luteum (a cyst on the ovary during pregnancy), but between 8 and 12 weeks the placenta takes over this role and maintains the pregnancy thereafter.[1] Mifepristone binds with high affinity to progesterone receptors,[2] thereby blocking the action of progesterone, resulting in fetal death in most cases.

12. Misoprostol, a prostaglandin analogue, is then given 24–48 hours after mifepristone. It leads to uterine contractions to expel the fetus and gestational sac. Chemical abortions of this type are approved by the FDA for use through the 10th week of gestation.

13. When we consider the risks and benefits of counteracting this kind of abortion, it is important to understand the risks of completing it. While 97.4% of women did not have viable (ongoing) pregnancies after taking both drugs at up to 10 weeks gestation,[3] that same study showed that, at that same gestational age, nearly 8% of women did not fully expel the fetus and other pregnancy tissue, which means that those patients would require a surgical procedure to complete their abortion.[4]

14. That study also showed that nearly 14% of women who took this drug combination from 10–11 weeks required surgical intervention.[5] This is consistent with larger studies, which show that the farther along in pregnancy a woman is when

[1] Coomarasamy A, Williams H, Truchanowicz E, et al. PROMISE: first-trimester progesterone therapy in women with a history of unexplained recurrent miscarriages – a randomized, double-blind, placebo-controlled, international multicenter trial and economic evaluation. Southampton (UK): NIHR Journals Library; 2016 May. (Health Technology Assessment, No. 20.41.) Chapter 1, Introduction. Available from: https://www.ncbi.nlm.nih.gov/books/NBK362730/.
[2] Heikinheimo O, Kekkonen R, Lähteenmäki P. The pharmacokinetics of mifepristone in humans reveal insights into differential mechanisms of antiprogestin action. Contraception. 2003 Dec;68(6):421-6. doi: 10.1016/s0010-7824(03)00077-5. PMID: 14698071.
[3] Ilana G. Dzuba et al., A Non-Inferiority Study of Outpatient Mifepristone-Misoprostol Medical Abortion at 64-70 Days and 71-77 Days of Gestation, 101(5) Contraception 302-308 (2020).
[4] *Id.*
[5] *Id.*

she takes these drugs, the higher her risk of complications.[6] In fact, a large registry-based study out of Finland (more robust and reliable than relying on self-reporting of patients or by abortion providers) that evaluated all women undergoing chemical and surgical abortions from 2000–06 (over 42,000 women total) showed that chemical abortions had a four times higher overall complication rate than surgical abortions.[7] The chemical abortion regimen is far from safe.

15. Claims that mifepristone is "safer than Tylenol" have no basis in reality. First, acetaminophen (Tylenol) toxicity is nearly exclusively caused by overdose—not taking the FDA-approved dose.[8] Mifepristone- and misoprostol-induced abortion has a four times higher complication rate than surgical abortion (see above) at the dosages approved by the FDA and prescribed to patients.[9] Second, mifepristone still has a black box warning attached to it due to the risk of hemorrhage and infection (specifically sepsis from Clostridium sordellii which causes an insidious sepsis picture and has caused the deaths of several women who took mifepristone).[10] Tylenol has no such warning. Finally, the FDA's own data shows that approximately 1 in 25 women who take mifepristone for an induced abortion will end up seeking care for complications in the emergency department—and this was when women were still being evaluated in person prior to receiving this[11].

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[6] Maarit J. Mentula, Maarit Niinimäki, Satu Suhonen, Elina Hemminki, Mika Gissler, Oskari Heikinheimo, Immediate adverse events after second trimester medical termination of pregnancy: results of a nationwide registry study, Human Reproduction, Volume 26, Issue 4, April 2011, Pages 927–932, https://doi.org/10.1093/humrep/der016.

[7] Niinimäki M, Pouta A, Bloigu A, Gissler M, Hemminki E, Suhonen S, Heikinheimo O. Immediate complications after medical compared with surgical termination of pregnancy. Obstet Gynecol. 2009 Oct;114(4):795-804. doi: 10.1097/AOG.0b013e3181b5ccf9. PMID: 19888037.

[8] Agrawal S, Khazaeni B. Acetaminophen Toxicity. [Updated 2023 Jun 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441917/.

[9] Niinimäki *et al.*, *supra* n.7.

[10] https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5429a3.htm.

[11] *Highlights of Prescribing Information, MIFEPREX (mifepristone) tablets, for oral use*, U.S. Food and Drug Administration (Mar. 2016), https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf

16. Abortion pill reversal (APR) is based on the scientific principle of reversible competitive inhibition. A brief explanation of this biochemical concept is warranted, as it undergirds the rationale behind APR:

> A competitive inhibition occurs when the drug, as 'mimic' of the normal substrate competes with the normal substrate for the active site on the enzyme. Concentration effects are important for competitive inhibition…A reversible inhibitor inactivates an enzyme through noncovalent, more easily reversed, interactions. Unlike an irreversible inhibitor, a reversible inhibitor can dissociate from the enzyme. Reversible inhibitors include competitive inhibitors and noncompetitive inhibitors…Probably the easiest type of enzyme inhibition to understand is competitive inhibition and it is the one most commonly exploited pharmaceutically. Molecules that are competitive inhibitors of enzymes resemble one of the normal substrates of an enzyme. An example is methotrexate, which resembles the folate substrate of the enzyme dihydrofolate reductase (DHFR). This enzyme normally catalyzes the reduction of folate, an important reaction in the metabolism of nucleotides. When the drug methotrexate is present, some of the enzyme binds to it instead of to folate and during the time methotrexate is bound, the enzyme is inactive and unable to bind folate. Thus, the enzyme is inhibited. Notably, the binding site on DHFR for methotrexate is the active site, the same place that folate would normally bind. As a result, methotrexate 'competes' with folate for binding to the enzyme. The more methotrexate there is, the more effectively it competes with folate for the enzyme's active site. Conversely, the more folate there is, the less of an effect methotrexate has on the enzyme because folate outcompetes it.[12]

17. In the context of APR, mifepristone is analogous to methotrexate, and progesterone is analogous to folate. Specifically, APR seeks to displace mifepristone from progesterone receptors using natural progesterone, thus counteracting the effects of mifepristone. Because mifepristone and progesterone compete for the same receptors, high amounts of substrate (in this case, progesterone) can displace the introduced competitive inhibitors (mifepristone) and therefore allow for normal placental development and growth of the fetus.

[12]https://chem.libretexts.org/Courses/University_of_Arkansas_Little_Rock/CHEM_4320_5320%3A_Biochemistry_1/05%3A_Michaelis-Menten_Enzyme_Kinetics/5.4%3A_Enzyme_Inhibition.

18. APR is suitable for pregnant women who have taken mifepristone but who have not yet taken the second drug, misoprostol. For women who have begun APR therapy and have a viable pregnancy, my practice is to continue progesterone through the end of the 12th week, at which time the placenta is developed and fully takes over progesterone production.

19. Women typically access APR treatment by calling the hotline number, which is staffed around the clock by nurses who conduct an initial screening for the appropriateness of APR. If the patient is deemed suitable for APR and desires to proceed, the nurse connects her to a local APR provider.

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

20. Empirical evidence supports that APR is effective in reversing the effects of mifepristone. A study by Das and Catt published in *Lancet* in 1987, when mifepristone was being developed, showed that the effect of mifepristone was reversed with the addition of exogenous progesterone.[13] In the largest direct study of APR to date, Dr. George Delgado and Dr. Mary Davenport examined 754 cases (547 women were included in the final analysis) where women attempted reversal of chemical abortion.[14] The study found an overall fetal survival rate following APR of 48%, with rates rising to 64% and 68% respectively for intramuscular and oral administration of progesterone.[15] The oral regimen involved women receiving a 400-

[13] Das C, Catt KJ. Antifertility actions of the progesterone antagonist RU 486 include direct inhibition of placental hormone secretion. Lancet. 1987 Sep 12;2(8559):599-601. doi: 10.1016/s0140-6736(87)92988-6. PMID: 2887889.

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

[15] *Id.* The latest version of the Delgado study clearly states that "[t]he study was reviewed and approved by an institutional review board." Although the Delgado study was briefly withdrawn over a

milligram dose of progesterone twice daily for three days, followed by 400 milligrams daily.[16] Because of its higher effectiveness rate and tolerability by patients, I use the oral regimen of progesterone.

21. This probable causal relationship of progesterone on pregnancy continuation after mifepristone ingestion was also shown in a randomized controlled trial that evaluated women who were given depot medroxyprogesterone acetate (a progesterone injectable contraceptive) at the time of a mifepristone induced abortion.[17] This study showed a statistically significant increase in ongoing pregnancy in women given the progesterone injection at the time of their abortion.[18]

22. When women took neither misoprostol nor progesterone after taking mifepristone, a 2017 study by Dr. Davenport found a fetal survival rate—not merely incomplete abortions—of 10–23%.[19] (Claims that fetal survival after mifepristone alone are as high as 50% are using data from studies that documented incomplete abortions, or retained tissue, not actual ongoing viable pregnancies.)[20] This study was used as a historical control group for the Delgado and Davenport 2018 study on APR,

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previous granting of institutional review board exemption, the article has since been reviewed and restored.

[16] *Id.*

[17] Raymond EG, Weaver MA, Louie KS, Tan YL, Bousiéguez M, Aranguré-Peraza AG, Lugo-Hernández EM, Sanhueza P, Goldberg AB, Culwell KR, Kaplan C, Memmel L, Sonalkar S, Jamshidi R, Winikoff B. Effects of Depot Medroxyprogesterone Acetate Injection Timing on Medical Abortion Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. Obstet Gynecol. 2016 Oct;128(4):739-45. doi: 10.1097/AOG.0000000000001627. PMID: 27607859.

[18] *Id.*

[19] Mary L. Davenport et al., Embryo Survival After Mifepristone: A Systematic Review of the Literature, 32 Issues L. & Med. 3, 3(2018). This result was also confirmed by a study in Contraception. *See* Mark A, Grossman D, Foster AM, Prager SW, Winikoff B. When patients change their minds after starting an abortion: Guidance from the National Abortion Federation's Clinical Policies Committee. Contraception. 2020 May;101(5):283-285. doi: 10.1016/j.contraception.2020.01.016. Epub 2020 Feb 5. PMID: 32035097.

[20] *Id.*

where it was shown that, so long as the progesterone is taken within 72 hours of the administration of mifepristone, the chances of fetal survival increases from 23% to as high as 68% (with the oral progesterone regimen).[21] This result is consistent with the pharmacokinetics of mifepristone—the drug does not immediately kill the fetus, instead starving it of nutrition over the course of days. It was also found that survival rates increased with gestational age, again consistent with the literature available on the efficacy of mifepristone for pregnancy termination by gestational age.[22]

23. The Delgado 2018 study has been criticized because it uses a historical control group rather than a randomized controlled trial, but it is well established in medical research that there are situations in which a historical control group is not only acceptable but also preferable. An article in the September 2023 issue of the Journal of the American Medical Association (one of the most prestigious peer-reviewed medical journals in the United States) addressed this issue specifically and states:

> [T]here are situations in which randomizing participants to a control treatment or placebo within an RCT may not be practical or ethical, e.g., if a comparison with placebo is desired but an effective treatment already exists. In such cases, researchers might use data from participants who had received the intended control treatment in a prior study, termed historical controls, to estimate the benefit of the new treatment.[23]

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[21] *Id.*

[22] Kapp N, Andersen K, Griffin R, Handayani AP, Schellekens M, Gomperts R. Medical abortion at 13 or more weeks gestation provided through telemedicine: A retrospective review of services. Contracept X. 2021 Jan 25;3:100057. doi: 10.1016/j.conx.2021.100057. PMID: 33615210; PMCID: PMC7881210.

[23] Marion JD, Althouse AD. The Use of Historical Controls in Clinical Trials. JAMA. 2023;330(15):1484–1485. doi:10.1001/jama.2023.16182.

It goes on to highlight why, in situations such as counteracting the effects of a mifepristone-induced abortion, a historical control group is particularly appropriate: "Historical controls are also used for diseases with particularly severe outcomes or that affect vulnerable populations such as children. Here, randomization may be viewed as unacceptable, even in the absence of a proven effective treatment."[24]

24. Adding to the body of literature showing that progesterone can counteract the effects of mifepristone, a recent paper by Turner *et al*. in *The Journal of Obstetrics and Gynecology Research* reported the results of the PAMper trial.[25] While a small study, this prospective single-arm pilot trial evaluated six women who took progesterone to counteract mifepristone when they changed their mind about completing the abortion.[26] They were all between 40 and 70 days gestation when they took mifepristone and started progesterone between 5.7 and 72 hours after mifepristone ingestion.[27] Five out of the six women had viable pregnancies after 2 weeks of progesterone treatment and there were no significant adverse events noted.[28]

25. Delgado's and Turner's findings are well-explained by biological theory. The principle behind these findings—that the effects of a competitive inhibitor can be undone by greater amounts of substrate—is firmly established. Even some pro-choice experts agree that this theory is sound. Dr. Harvey Kliman of the Yale School of

[24] *Id.*
[25] Turner, JV, Garratt, D, McLindon, LA, Barwick, A, Spark, MJ. Progesterone after mifepristone: A pilot prospective single arm clinical trial for women who have changed their mind after commencing medical abortion. J Obstet Gynaecol Res. 2023. https://doi.org/10.1111/jog.15826.
[26] *Id.*
[27] *Id.*
[28] *Id.*

Medicine, who has supported pro-choice causes, admits that mifepristone reversal makes "biological sense."[29] Accordingly, he said that if one of his daughters mistakenly ingested mifepristone, he would recommend 200 milligrams of progesterone three times a day until mifepristone is metabolized.[30]

26. There are other studies that support the fact that mifepristone is a reversible inhibitor of progesterone. In a 1989 study by Yamabe, scientists separated pregnant rats into three groups.[31] The first group received no drugs; the second group received mifepristone; the third group received mifepristone followed by natural progesterone.[32] Of the no-drug group, 100% of the animals delivered live offspring.[33] The mifepristone group, as would be expected, had a significantly lower live birth rate, with only 33% delivering live offspring.[34] However, in the group that received progesterone after mifepristone, 100% delivered live offspring.[35]

27. Recently (early 2023), Camilleri and Sammut published research on progesterone-mediated reversal of mifepristone in rats that specifically looked at survival of the fetus to term.[36] The results of this study showed that all fetuses survived in the normal pregnant group (no mifepristone administered), no fetuses

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[29] Ruth Graham, A New Front in the War Over Reproductive Rights: 'Abortion Pill Reversal,' N.Y. Times Mag. (July 18, 2017), https://www.nytimes.com/2017/07/18/magazine/a-new-front-in-the-war-over-reproductive-rights-abortion-pill-reversal.html?auth=login-google1tap&login=google1tap.

[30] *Id.*

[31] Yamabe S, Katayama K, Mochizuki M. [The effect of RU486 and progesterone on luteal function during pregnancy]. Nihon Naibunpi Gakkai Zasshi. 1989 May 20;65(5):497-511. Japanese. doi: 10.1507/endocrine1927.65.5_497. PMID: 2776921.

[32] *Id.*

[33] *Id.*

[34] *Id.*

[35] *Id.*

[36] Camilleri, C., Sammut, S. Progesterone-mediated reversal of mifepristone-induced pregnancy termination in a rat model: an exploratory investigation. Sci Rep 13, 10942 (2023). https://doi.org/10.1038/s41598-023-38025-9.

survived in the abortion group (mifepristone administered but no progesterone), and 13 of 16 (81%) of the fetuses in the progesterone group survived (progesterone administered after mifepristone).[37] Of note, this occurred at the equivalent of 4–6 weeks gestation in humans—a time when mifepristone (as previously noted) is known to be highly effective in producing fetal death.[38]

28. It is important to note that mice and rats have been used for decades in biomedical research due to their anatomical, physiological, and genetic similarity to humans.[39]

29. Mifepristone binding to another hormonal receptor, glucocorticoid receptors, has also been shown to be reversible by the addition of glucocorticoids.[40]

30. While mifepristone has a higher relative binding affinity (binds more tightly) to the progesterone receptor than progesterone,[41] just because a competitive inhibitor binds to a receptor with tight affinity does not mean it can't be displaced. The perfect example of this is carbon monoxide poisoning and its treatment. Carbon monoxide is a competitive inhibitor of oxygen at a hemoglobin binding site (like mifepristone is to progesterone at the progesterone receptor). It binds to this site with a 240 times greater affinity than oxygen (as compared to mifepristone which binds

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[37] *Id.*
[38] *Id.*
[39] Bryda EC. The Mighty Mouse: the impact of rodents on advances in biomedical research. Mo Med. 2013 May-Jun;110(3):207-11. PMID: 23829104; PMCID: PMC3987984.
[40] JI Webster & EM Sternberg, Role of the hypothalamic-pituitary-adrenal axis, glucocorticoids and glucocorticoid receptors in toxic sequelae of exposure to bacterial and viral products, 181 J. ENDOCRINOLOGY 212 (2004).
[41] Heikinheimo O, Kekkonen R, Lähteenmäki P. The pharmacokinetics of mifepristone in humans reveal insights into differential mechanisms of antiprogestin action. Contraception. 2003 Dec;68(6):421-6. doi: 10.1016/s0010-7824(03)00077-5. PMID: 14698071.

with a 2.3 times greater affinity than progesterone).[42] However, it can be displaced from its binding site with the administration of high doses of oxygen. In fact, hyperbaric oxygen treatment is one of the mainstays of treatment for carbon monoxide toxicity.[43]

31. It is a common practice in medicine to give an agent to counteract a lethal ingestion. Another example of this is administering Narcan to counteract the effects of a lethal overdose of fentanyl or other opioids. Narcan counteracts the effects of the opioid by displacing it from the opioid receptor.[44]

D. APR is Safe for Pregnant Women and Fetuses.

32. There is no documented risk that mifepristone exposure or APR leads to increased incidence of birth defects. Multiple studies have shown that neither progesterone nor mifepristone are associated with an increased risk of birth defects.

33. A study published in the British Journal of Obstetrics and Gynaecology, an international journal of obstetrics and gynecologists, found that the incidence of birth defects in children exposed to mifepristone in the first trimester was equivalent to the incidence in the general population.[45] Delgado's 2018 study similarly found no increased risk of birth defects.[46] Further, according to the package insert for mifepristone, no teratogenic effects have been noted in experiments with rats and

[42] Manaker S, Perry H. Carbon monoxide poisoning. In: UpToDate, Topic 322 Version 51.0; UpToDate, Waltham MA. (Accessed on Nov. 12, 2023).
[43] Crawford Mechem C, Manaker S. Hyperbaric oxygen therapy. In: UpToDate, Topic 326 Version 30.0; UpToDate, Waltham MA. (Accessed on Nov. 12, 2023).
[44] Jordan MR, Morrisonponce D. Naloxone. [Updated 2023 Apr 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441910/.
[45] N. Bernard et al., Continuation of Pregnancy After First-Trimester Exposure to Mifepristone: An Observational Prospective Study, 120 BJOG 568 (2013).
[46] Delgado *et al.*, *supra* n.15.

mice.[47] These are studies that AG James ignores in paragraphs 141–143 of her claim that HBI is misleading women when they state there is no increased risk of birth defects from the APR protocol. A birth defect—Mobius syndrome—is known to occur when fetuses are exposed to misoprostol[48] (the second drug in the two-drug regimen), but this is distinct from and unrelated to mifepristone exposure.

34. Natural progesterone has been safely used during pregnancy for over 50 years, notably to support IVF pregnancies and in women who have a history of pregnancy loss.[49]

35. In 1999, the FDA conducted a comprehensive review of relevant scientific literature and concluded that there was no increased risk of birth defects associated with the use of progesterone and that the "use of [progesterone] for luteal phase support in IVF cycles had become routine and that the agency had itself recently approved a [progesterone] gel for use in infertile women under treatment with ART."[50]

36. The American Society for Reproductive Medicine (ASRM) concluded in a bulletin on progesterone supplementation during pregnancy: "The weight of

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[47] FDA, MIFEPREX Prescribing Information, at 9 (2016), https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/020687s020lbl.pdf.

[48] A.L. Pastuszak, *Use of Misoprostol During Pregnancy and Möbius' Syndrome in Infants*, 338 N. Eng. J. Med. 1881, 1882–83 (1998).

[49] Coomarasamy A, Williams H, Truchanowicz E, 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*. Southampton (UK): NIHR Journals Library; 2016 May. (Health Technology Assessment, No. 20.41.) Chapter 1, Introduction. Available from: https://www.ncbi.nlm.nih.gov/books/NBK362730/.

[50] 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).

available evidence indicates that the most common forms of [progesterone] supplementation during early pregnancy pose no significant risk to mother or fetus."[51] This is in direct contradiction to AG James' claims in paragraphs 141–143 that HBI's claims that progesterone is safe and does not cause an increased risk of birth defects are misleading.

37. The UK's National Institute of Health and Care Excellence (NICE) published new guidelines in 2021 recommending progesterone therapy for women with early pregnancy bleeding and at least one previous miscarriage.[52] This recommendation followed a Cochrane review of studies on progesterone use in early pregnancy.[53] NICE's chief executive, Gillian Leng, 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."[54]

38. Although the FDA has yet to approve the use of progesterone in the specific context of APR, off-label use of medications is common, even in pregnancy, when they have been safely used in clinical practice. One example is that the American College of Obstetricians and Gynecologists (ACOG) recommends off-label use of misoprostol as first-line therapy for cervical ripening for term induction of

[51] *Id.*
[52] *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).
[53] *Id.*
[54] BMJ 2021;375:n2896 http://dx.doi.org/10.1136/bmj.n2896 Published: 24 November 2021.

labor.[55] Giving progesterone to women in the first trimester of pregnancy is not experimental and is backed by more than 50 years of clinical experience.

E. Addressing Common Criticisms of APR.

39. Critics of APR often focus on the lack of randomized placebo-controlled trials (RCT) on mifepristone reversal, but they overlook the fact that such studies would be unethical. It would be contrary to medical ethics to administer a placebo to a patient seeking to reverse the feticidal effects of mifepristone when we know through clinical experience, animal trials, and basic pharmacology that progesterone is safe and effective in this scenario.

40. Where an RCT is not possible for ethical or other reasons, historical control groups, as were used in Delgado's study, are an acceptable alternative.[56]

41. Tellingly, none of the trials relied on in the approval of mifepristone were RCTs—they either used a historical control group or were dose comparison studies. As the FDA's statistical review of the application for mifepristone approval stated: "In the absence of a concurrent control group in each of these studies, it is a matter of clinical judgment whether or not the sponsor's proposed therapeutic regimen is ... viable."[57]

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[55] ACOG Practice Bulletin No. 107: Induction of Labor, 114 Obstetrics & Gynecology 386 (2009), https://journals.lww.com/greenjournal/citation/2009/08000/acog_practice_bulletin_no__107__induction_of_labor.30.aspx.

[56] *Marian et al.*, *supra* n.27.

[57] FDA, *Statistical Review and Evaluation of Mifepristone 7–8* (1996) quoted in Byron C. Calhoun & Donna J. Harrison, *Challenges to the FDA Approval of Mifepristone*, 38 Annals of Pharmacotherapy 163, 164 (2004).

42. The one attempted RCT study on APR, conducted by Mitchell Creinin et al., was stopped at an early stage due to "safety concerns."[58] Creinin, an abortion provider from the pro-abortion Bixby Center at the University of California San Francisco, conducted an experiment where women were given mifepristone, followed by either progesterone or a placebo, but not given misoprostol. They were scheduled to follow up two weeks later for an ultrasound, where investigators would determine whether they had an ongoing, viable pregnancy. If they had an ongoing pregnancy, the fetus would then be surgically aborted.

43. The study included five women in the final treatment group who were administered progesterone and five in the final control group who were not administered progesterone. The trial was halted after three women required emergency room visits.[59] Of these three women, only one woman was from the progesterone treatment group, and she was found to be completing her abortion and required no treatment.[60] The other two women were from the placebo group—both presented with heavy vaginal bleeding and required emergency dilation and curettage. One of the two received a blood transfusion.[61] Therefore, it cannot be said that the safety concerns that halted the study are related to the administration of progesterone following mifepristone without misoprostol.[62] In fact, the significant adverse effect of heavy bleeding and retained tissue almost certainly originated from

[58] Mitchell D. Creinin et al., *Mifepristone Antagonization with Progesterone to Prevent Medical Abortion: A Randomized Controlled Trial*, 135 Obstetrics & Gynecology 158, 158 (2020).
[59] *Id.* at 160–61.
[60] *Id.*
[61] *Id.*
[62] *Id.*

the administration of mifepristone, which is known to increase risk of hemorrhage due to its effect on the spiral arteries of the pregnant uterus.[63] It is thus misleading to cite the Creinin study to demonstrate that APR is dangerous.

44. The Creinin study also does not disprove, but actually supports the effectiveness of APR. In the placebo group, two out of five women had ongoing pregnancy (40% survival). In the progesterone treatment group, however, four out of five women had ongoing pregnancies (80% survival).

45. It is not surprising that ACOG has not endorsed APR. ACOG has a long history of promoting a pro-abortion agenda and opposing abortion safety regulations.[64] Even the most basic safety restriction, like requiring a physician who performs surgical abortions to have the ability to admit patients with complications to get additional care, has not been supported by ACOG.

46. ACOG has ignored the wealth of evidence that progesterone can be used to counteract the effects of mifepristone and help women who regret beginning an abortion to potentially save their child.

47. Truly informed consent to undergo a chemical abortion requires disclosure of APR. By denying information about APR to a woman who would otherwise seek it, opponents are essentially consigning that woman to completing an abortion she no longer desires and preventing her from trying to save her child. This

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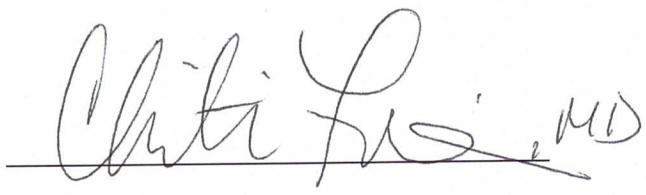
[63] Miech RP. *Pathopharmacology of excessive hemorrhage in mifepristone abortions*. Ann Pharmacother. 2007 Dec;41(12):2002-7. doi: 10.1345/aph.1K351. Epub 2007 Oct 23. PMID: 17956963.
[64] ACOG has filed amicus briefs on behalf of pro-abortion causes at the expense of sound medical judgment. *See, e.g.*, Brief of Amicus Curiae Am. Assoc. of Pro-Life Obstetricians and Gynecologists in Support of Rebekah Gee, Secretary, Louisiana Dep't. of Health and Hosps., *June Med. Services L.L.C. v. Gee*, 905 F.3d 787 (5th Cir. 2018).

is impermissible no matter how many women regret their abortion choice—whether it is only a few or many. Abortion proponents, such as the National Abortion Federation, currently state that if a woman changes her mind after taking mifepristone, she should do nothing[65] (rather than take progesterone). However, as noted in a recent systematic review of studies on reversal of medication abortion by progesterone[66] and highlighted by the Creinin study, there are "safety concerns with not taking misoprostol after mifepristone" in patients who do not take progesterone.

48. The medical evidence demonstrates that not only is counteracting the effects of mifepristone with progesterone (APR) scientifically feasible, but it has also been supported by sound clinical experience and scientific testing. Accordingly, it is unethical to withhold this potentially life-saving treatment from women who are seeking it for the purposes of counteracting a mifepristone-induced abortion.

I declare under penalty of perjury that the foregoing is true and correct. Executed on May 24, 2024.



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[65] Mark A, Grossman D, Foster AM, Prager SW, Winikoff B. *When patients change their minds after starting an abortion: Guidance from the National Abortion Federation's Clinical Policies Committee.* Contraception. 2020 May;101(5):283-285. doi: 10.1016/j.contraception.2020.01.016. Epub 2020 Feb 5. PMID: 32035097.

[66] Stifani BM, Lavelanet AF *Reversal of medication abortion with progesterone: a systematic review.* BMJ Sexual & Reproductive Health Published Online First: 20 October 2023. doi: 10.1136/bmjsrh-2023-201875.