IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

REGENXBIO Inc.,
9600 Blackwell Road, Suite 210
Rockville, MD 20850,

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION,
10903 New Hampshire Avenue
Silver Spring, MD 20993;

ALEX M. AZAR II, in his official capacity as Secretary of Health and Human Services,
200 Independence Avenue, S.W.
Washington, DC 20201;

BRETT GIROIR, in his official capacity as Acting Commissioner of Food and Drugs,
10903 New Hampshire Avenue
Silver Spring, MD 20993;

EDWARD THOMPSON, in his official capacity as Regulatory Project Manager at Food and Drug Administration,
10903 New Hampshire Avenue
Silver Spring, MD 20993;

THE UNITED STATES OF AMERICA,

Defendants.

Civil Case. No. 1:19-cv-3373

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff REGENXBIO Inc. ("REGENXBIO"), by and through its undersigned attorneys, alleges as follows:

INTRODUCTION

1. REGENXBIO challenges the Food and Drug Administration's ("FDA") clinical hold order on its potentially life-changing treatment for retinal diseases that lead to blindness. FDA's final agency action is contrary to law and arbitrary and capricious because it did not follow the statute or its own regulations, nor did FDA offer a reasoned explanation for issuing a clinical hold without advance warning. The clinical hold also violates the Fifth Amendment's Due Process Clause by depriving REGENXBIO of a protected interest without even the most basic procedural protections. In addition, Section 505(i)(3)(B)(ii) of the of the Federal Food, Drug, and Cosmetic Act ("FDCA")—which authorizes FDA to issue clinical hold orders—is unconstitutional because it delegates unfettered discretion to FDA to issue a clinical hold order for "such other" extra-statutory "reasons as [FDA] may by regulation establish." 21 U.S.C. § 355(i)(3)(B)(ii).

2. REGENXBIO was founded with the goal of improving lives through the curative potential of gene therapy. To that end, REGENXBIO has invested tens of millions of dollars in developing gene therapy for the treatment of retinal and other diseases. Most recently, REGENXBIO developed RGX-314 to treat the leading cause of blindness in the United States, wet age-related macular degeneration. The results of an interim clinical trial for RGX-314 were promising: RGX-314 was well tolerated by all forty-two patients, with patients at the higher doses tested experiencing stable to improved vision on average and an overall reduction in the need for alternative treatments to halt the course of the disease. Based on these results and discussions with FDA, REGENXBIO was on track to begin the next phase of clinical trials for RGX-314 before the end of 2019.

3. But on October 18, 2019, without notice or explanation, FDA placed RGX-314 on a clinical hold, effectively halting REGENXBIO's development of this potentially life-altering treatment for retinal diseases that are leading causes of adult blindness. Since issuing the clinical

hold order, FDA has rebuffed REGENXBIO's repeated attempts to obtain an explanation of the basis for the clinical hold.

4. By failing to provide advance notice of, or any reasoned basis for, the clinical hold, FDA violated the FDCA and its own regulations. FDA's clinical hold on RGX-314 is therefore contrary to law and arbitrary and capricious under the Administrative Procedure Act ("APA").

5. FDA's clinical hold also violates the Fifth Amendment's Due Process Clause because it deprives REGENXBIO of a protected interest without notice or an opportunity to be heard.

6. In addition, Section 505(i)(3)(B)(ii) of the FDCA—pursuant to which FDA issued the clinical hold in this case—is an unconstitutional delegation of legislative authority from Congress to the Executive. The statute gives the Secretary of Health and Human Services unfettered discretion to promulgate regulations governing when a drug may be placed on clinical hold, but it fails to provide any intelligible principle to guide the Secretary's discretion. The Court should declare this provision of the FDCA unconstitutional and enjoin its enforcement.

JURISDICTION AND VENUE

7. This Court has jurisdiction over this case pursuant to 28 U.S.C. § 1331 because the claims arise under the APA and the United States Constitution. *See* 5 U.S.C. § 701.

8. The Court has authority to grant declaratory relief and to vacate and set aside the clinical hold pursuant to the Declaratory Judgment Act, the APA, and the Court's inherent equitable powers. *See* 28 U.S.C. § 2201; 5 U.S.C. §§ 702, 706.

9. Venue is proper in this district pursuant to 28 U.S.C. § 1391(e)(1)(A).

10. FDA's clinical hold order is final agency action because it is the consummation of the agency's decisionmaking process with regard to RGX-314, and it affects REGENXBIO's right to continue clinical trials of RGX-314. *See* 21 C.F.R. § 312.42.

11. REGENXBIO has standing because it is suffering reputational, economic, and competitive injury caused by FDA's clinical hold order, and those injuries are redressable by a court order setting aside the clinical hold.

PARTIES

12. Plaintiff REGENXBIO is a biotechnology company focused on the development, commercialization, and licensing of recombinant adeno-associated virus gene therapy. REGENXBIO is a corporation duly organized and existing under the laws of the state of Delaware with its principal place of business in in Rockville, Maryland.

13. Defendant FDA is an agency of the United States within the Department of Health and Human Services with offices at 200 Independence Avenue, SW, Washington, DC, and 10903 New Hampshire Avenue, Silver Spring, MD. The Secretary has delegated to FDA the authority to administer the relevant provisions of the FDCA.

14. Defendant Alex M. Azar II is Secretary of Health and Human Services and is charged by law with administering the FDCA. He is sued in his official capacity. Secretary Azar maintains an office at 200 Independence Avenue, SW, Washington, DC.

15. Defendant Brett Giroir is the Acting Commissioner of Food and Drugs and is the senior official at FDA. He is sued in his official capacity. Dr. Giroir maintains offices at 200 Independence Avenue, SW, Washington, DC, and 10903 New Hampshire Avenue, Silver Spring, MD.

16. Defendant Edward Thompson is Regulatory Project Manager at FDA. He is sued in his official capacity. Mr. Thompson maintains offices at 200 Independence Avenue, SW, Washington, DC, and 10903 New Hampshire Avenue, Silver Spring, MD.

17. Defendant the United States of America is the federal government, acting through FDA, which is an agency of the United States, and its officials. The United States is named as a defendant pursuant to 5 U.S.C. § 702.

STATEMENT OF FACTS

I. Regulatory Framework

18. While the FDCA generally prohibits the introduction of drugs into interstate commerce absent FDA approval, the Act creates a limited exception to permit the study of new drugs prior to their approval. *See* 21 U.S.C. §§ 355(a), 331(d). Section 505(i)(1) of the FDCA

accordingly provides that "drugs intended solely for investigational use by experts" are exempt from the prohibition on unapproved drugs in commerce. 21 U.S.C. §§ 355(i)(1). It also authorizes the Secretary to promulgate regulations for this exemption.

19. These regulations permit investigational new drugs to be used in clinical investigations if, among other things, the sponsors of the investigations submit investigational new drug applications to the FDA. 21 C.F.R. § 312.40(a)(1). An investigational new drug must become effective before clinical trials in the United States may begin. *Id.*

20. At any point during the course of clinical development of a new drug, FDA "may prohibit the sponsor of an investigation from conducting the investigation." 21 U.S.C. § 355(i)(3)(A). This prohibition is known as a "clinical hold." *Id.* The FDCA provides that a clinical hold may be imposed if FDA determines either that (1) "the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation" or (2) "the clinical hold should be issued for such other reasons as the Secretary may by regulation establish." *Id.* § 355(i)(3)(B)(i), (ii).

21. The Secretary has promulgated regulations governing the issuance of clinical holds. As relevant here, 21 C.F.R. § 312.42 authorizes FDA to issue a clinical hold on an investigational new drug application if it finds that: (1) human subjects are or would be exposed to an unreasonable and significant risk of illness or injury; (2) the clinical investigators named in the investigational new drug application are not qualified by reason of their scientific training and experience to conduct the investigation described in the investigational new drug application; (3) the investigator brochure is misleading, erroneous, or materially incomplete; (4) the investigational new drug application does not contain sufficient information required under § 312.23 to assess the risks to subjects of the proposed studies; or (5) the plan or protocol for the investigation is clearly deficient in design to meet its stated objectives. 21 C.F.R. § 312.42(b)(1)(i)–(iv), (b)(2)(i)–(ii).

22. When FDA concludes that a deficiency exists in a clinical investigation, and that this deficiency may be grounds for imposing a clinical hold, FDA is required first to "attempt to

discuss and satisfactorily resolve the matter with the sponsor before issuing the clinical hold order," unless "patients are exposed to immediate and serious risk." *Id.* § 312.42(c).

23. While a clinical hold order "may be made by telephone or other means of rapid communication or in writing," all clinical hold orders are required to "briefly explain the basis for the action." *Id.* § 312.42(d); *see also* 21 U.S.C. § 355(i)(3)(A) ("Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold.").

II. The Clinical Hold on REGENXBIO's Investigational New Drugs

24. Prior to FDA issuing the clinical hold, REGENXBIO submitted two investigational new drug applications for its potentially life-changing treatment of retinal diseases that lead to blindness called RGX-314: IND 17280 and IND 19210.

25. IND 17280 is for the treatment of wet age-related macular degeneration, which is characterized by loss of vision due to excess blood vessel formation between two layers of cells in the eye's retina and is a leading cause of blindness in the United States. In the clinical trials performed to date, forty-two patients have been treated under this IND, with overall positive results.

26. IND 19210 is a more recent investigational new drug application for the treatment of diabetic retinopathy, which is a leading cause of blindness in the United States.

27. On October 18, 2019, Edward Thompson, FDA Regulatory Project Manager, notified REGENXBIO via voicemail and email that both IND 17280 and IND 19210 were on a full clinical hold, effective immediately. Mr. Thompson advised that, pursuant to this clinical hold order, "[s]tudy subjects in IND 17280 may not be given the investigational drug, no new subjects may be recruited to the study and administered the investigational drug; [and] patients already in the study should be taken off therapy involving the investigational drug unless specifically permitted by FDA in the interest of patient safety."

28. In his email, Mr. Thompson stated that FDA would issue a letter "outlining the deficiencies and information needed to remove the hold from the [investigational new drugs]" in

thirty days. Neither Mr. Thompson nor any other representative of FDA provided REGENXBIO with a reason for the hold.

29. In a subsequent email, Mr. Thompson stated that "[t]hese [investigational new drugs] are being placed on hold due to issues associated with their delivery systems" and that FDA is "working on addressing the device concerns." Mr. Thompson did not identify or explain these "issues" or "device concerns."

30. REGENXBIO subsequently requested details regarding the reason for the hold, but Mr. Thompson replied that he did "not have any comments to share at this time."

31. Despite REGENXBIO's repeated outreach to various individuals at FDA, the agency never provided any reason for the clinical hold.

32. On October 25, 2019, Rachael Anatol, the Deputy Director of FDA's Office of Tissues and Advanced Therapies, sent REGENXBIO an email clarifying that IND 17280 was on a *partial* clinical hold, whereby no new patients could be enrolled, but current patients could continue to be treated. She further clarified that IND 19210 was on a *full* clinical hold.

33. As a precautionary measure, and because FDA did not provide an explanation of the purported deficiencies with IND 19210, REGENXBIO withdrew IND 19210 on October 25, 2019, but the partial clinical hold on IND 17280 remains in effect.

34. On November 1, 2019, Dr. Anatol sent REGENXBIO an email noting that "FDA has received multiple communications, from various representatives of [REGENXBIO], regarding the reason for the partial hold for IND 17280 . . . . [FDA] will provide [REGENXBIO] a written explanation of the basis for the hold by the due date of 11/15/19."

35. FDA's actions have harmed, and continue to harm, REGENXBIO and the millions of American adults suffering from wet age-related macular degeneration and diabetic retinopathy by delaying the clinical development of these potentially vision-saving treatments. In addition to the reputational harm on REGENXBIO caused by the clinical hold, REGENXBIO is suffering actual and direct economic and competitive injury from the delay in development of these life-altering blindness treatments.

36. On November 5, 2019, REGENXBIO publicly disclosed FDA's clinical hold. In that disclosure, REGENXBIO stated that "we now plan to initiate our Phase IIb trial for RGX-314 in wet AMD and file our [investigational new drug application] for diabetic retinopathy in Q1 2020." REGENXBIO also noted that it has "not received reports of any device-related concerns or complications in the subjects already dosed in the Phase I/IIa trial" and that "[a]ssessments and monitoring of all enrolled subjects in the trial continue to be performed as usual." The day after REGENXBIO made this announcement, the value of its stock dropped by 3.93 percent.

CLAIMS FOR RELIEF

Count I – Violation of Administrative Procedure Act
FDA Lacks a Statutory Basis to Issue the Clinical Hold

37. REGENXBIO realleges and incorporates by reference the allegations contained in all of the preceding paragraphs as though set forth fully herein.

38. The partial clinical hold on IND 17280 and the full clinical hold on IND 19210 constitute "[a]gency action made reviewable by statute and final agency action for which there is no other adequate remedy in a court." 5 U.S.C. § 704.

39. A court must "hold unlawful and set aside agency action . . . found to be . . . not in accordance with law." 5 U.S.C. § 706(2)(A); *Cook v. FDA*, 733 F.3d 1, 11 (D.C. Cir. 2013).

40. In issuing the clinical hold, FDA acted contrary to law by failing to comply with the FDCA.

41. Section 505(i)(3)(A) of the FDCA directs that, in issuing a clinical hold, the Secretary "*shall* specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold." 21 U.S.C. § 355(i)(3)(A) (emphasis added).

42. FDA failed to comply with this statutory command. Despite REGENXBIO's multiple attempts to obtain an explanation for the clinical hold, the only information FDA has provided is a single statement that the hold relates to "issues associated with [the investigational

new drugs'] delivery systems." This cursory statement does not supply the "basis for the clinical hold" or the "specific information" required.

Count II – Violation of Administrative Procedure Act
FDA Lacks a Regulatory Basis to Issue the Clinical Hold

43. REGENXBIO realleges and incorporates by reference the allegations contained in all of the preceding paragraphs as though set forth fully herein.

44. A court must "hold unlawful and set aside agency action . . . found to be . . . not in accordance with law." 5 U.S.C. § 706(2)(A); *Cook*, 733 F.3d at 11.

45. In issuing the clinical hold, FDA acted contrary to law in violation of its own regulations.

46. FDA never "attempt[ed] to discuss and satisfactorily resolve the matter with" REGENXBIO "before issuing the clinical hold order," as required by 21 C.F.R. § 312.42(c). In fact, REGENXBIO was not aware that FDA had concerns with its investigational new drug applications until October 18, 2019, when FDA informed REGENXBIO via voicemail and email that IND 19210 and IND 17280 had been placed on clinical hold, effective immediately.

47. FDA "failed to briefly explain the basis" for the clinical hold order, as required by 21 C.F.R. § 312.42(d). Even where a clinical hold order is "made by telephone or other rapid means of communication," FDA must still "briefly explain the basis of the action." *Id.* Mr. Thompson's email did not contain a single reason for the clinical hold order, and despite REGENXBIO's multiple subsequent attempts to obtain an explanation for the hold, FDA has failed to provide an adequate basis for the clinical hold.

48. FDA failed to identify a permissible basis for the clinical hold order, as required by 21 C.F.R. § 312.42(b)(2). Section 312.42(b)(2) sets forth specific circumstances under which FDA may issue a clinical hold under Phase II. Neither "issues associated with . . . delivery" nor "device concerns" is a lawful reason for issuing a clinical hold.

Count III – Violation of Administrative Procedure Act
Arbitrary and Capricious Agency Action in Violation of the APA

49. REGENXBIO realleges and incorporates by reference the allegations contained in all of the preceding paragraphs as though set forth fully herein.

50. A court must "hold unlawful and set aside agency action . . . found to be . . . arbitrary, capricious, [or] an abuse of discretion." 5 U.S.C. § 706(2)(A); *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42–43, 52 (1983).

51. FDA's clinical hold order is arbitrary and capricious. Not only did FDA fail to articulate a rational explanation for its clinical hold, but FDA failed to provide any explanation at all.

Count IV – Violation of the United States Constitution
Deprivation of a Protected Interest without Due Process of Law

52. REGENXBIO realleges and incorporates by reference the allegations contained in all of the preceding paragraphs as though set forth fully herein.

53. A court must "hold unlawful and set aside agency action . . . found to be . . . contrary to constitutional right, power, privilege, or immunity." 5 U.S.C. § 706(2)(B).

54. The Fifth Amendment's Due Process Clause states: "No person shall . . . be deprived of life, liberty, or property, without due process of law." U.S. Const. amend. V. Where a government action deprives an individual of a protected life, liberty, or property interest, the Due Process Clause requires, at minimum, fair notice and an opportunity to be heard. *Mathews v. Eldridge*, 424 U.S. 319, 333 (1976).

55. REGENXBIO has a property interest in IND 17280 and IND 19210 and the associated right to investigate and develop RGX-314 through clinical trials. By imposing the clinical hold without providing REGENXBIO with notice or an opportunity to review and rebut any alleged reasons supporting the clinical hold, FDA deprived REGENXBIO of its protected property interest without due process of law.

56. In addition, REGENXBIO has a liberty interest in being free of reputational harm. The clinical hold harms REGENXBIO's reputation by falsely suggesting that RGX-314

creates an unreasonable risk to the safety of the persons participating in its clinical trials. By imposing the clinical hold without providing REGENXBIO with notice or an opportunity to review and rebut any alleged reasons supporting the clinical hold, FDA deprived REGENXBIO of its protected liberty interest without due process of law and adversely affected REGENXBIO's ability to develop one of its most important products.

Count V – Violation of the United States Constitution
Improper Delegation of Legislative Power to the Secretary of Health and Human Services

57. REGENXBIO realleges and incorporates by reference the allegations contained in all of the preceding paragraphs as though set forth fully herein.

58. A court must "hold unlawful and set aside agency action . . . found to be . . . contrary to constitutional right, power, privilege, or immunity." 5 U.S.C. § 706(2)(B).

59. The U.S. Constitution provides that "*[a]ll* legislative Powers herein granted shall be vested in a Congress of the United States." U.S. Const. art. I, § 1 (emphasis added). Under the nondelegation doctrine, Congress cannot delegate legislative power to the Executive Branch. *Gundy v. United States*, 139 S. Ct. 2116, 2123 (2019). Acts of Congress must supply an "intelligible principle" to guide the Executive Branch's discretion. *Id.*

60. Section 505(i)(3)(B)(ii) of the FDCA violates Article I's Vesting Clause and the separation of powers because Congress delegated legislative power to the Secretary with no "intelligible principle" to guide the Secretary's discretion. Section 505(i)(3)(B)(i) authorizes the Secretary to issue a clinical hold if "the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation." 21 U.S.C. § 355(i)(3)(B)(i). But Section 505(i)(3)(B)(ii) further authorizes the Secretary to issue a clinical hold "for such other reasons as the Secretary may by regulation establish." *Id.* § 355(i)(3)(B)(ii). Congress provided no intelligible principle to guide the Secretary's discretion to issue a clinical hold "for such other reasons" as the Secretary may determine.

PRAYER FOR RELIEF

Wherefore, REGENXBIO prays for the following relief:

1. A declaration, order, and judgment holding unlawful, enjoining, and setting aside the partial clinical hold on IND 17280 and the full clinical hold on IND 19210;

2. A declaration, order, and judgment holding that 21 U.S.C. § 355(i)(3)(B)(ii) is unconstitutional;

3. A preliminary and permanent injunction setting aside the partial clinical hold on IND 17280 and the full clinical hold on IND 19210 and enjoining FDA from enforcing 21 U.S.C. § 355(i)(3)(B)(ii).

4. An award of all costs and attorneys' fees pursuant to any applicable statute or authority;

5. Any other relief that this Court deems just and proper.

November 7, 2019

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that, on November 7, 2019, I electronically filed the foregoing documents with the Clerk of the Court for the United States District Court for the District of Columbia by using the CM/ECF system. I further certify that, on November 7, 2019, I caused the foregoing document to be sent via certified mail to:

Food and Drug Administration
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November 7, 2019

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