

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

GENZYME CORPORATION and AVENTIS
INC.,

Plaintiffs,

V.

NOVARTIS GENE THERAPIES, INC.
and NOVARTIS PHARMACEUTICALS
CORPORATION,

Defendants.

C.A. No. 21-1736-RGA

**REDACTED PUBLIC VERSION
FILED AUGUST 11, 2023**

**DEFENDANTS' REPLY BRIEF IN SUPPORT OF THEIR MOTION FOR LEAVE
TO AMEND THEIR ANSWER, DEFENSES, AND COUNTERCLAIMS**

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TABLE OF ABBREVIATIONS

Abbreviation	Description
'222 Provisional	Provisional Application No. 60/639,222
'542 Patent	U.S. Patent No. 9,051,542
'997 Provisional	Provisional Application No. 60/575,997
AAV	adeno-associated virus
Am. Ans.	Refers to Defendants' [Proposed] First Amended Answer, Defenses, and Counterclaims (D.I. 239, Exhibit A)
Ans. Ex. __	Refers to Exhibits to Defendants' [Proposed] First Amended Answer, Defenses, and Counterclaims (D.I. 239, Exhibit A at Exs. 1-8)
Ex. __	Refers to accompanying Exhibits to Defendants' Reply Brief In Support of Their Motion for Leave to Amend Their Answer, Defenses, and Counterclaims (Exs. 24-25)
Notebook 670	Avigen Laboratory Notebook No. 670
Novartis	Novartis Gene Therapies, Inc. and Novartis Pharmaceuticals Corporation
Opp.	Plaintiffs' Opposition to Defendants' Motion for Leave to Amend Their Answer, Defenses, and Counterclaims (D.I. 255)
Plaintiffs	Genzyme Corporation and Aventis Inc.
PTO	United States Patent and Trademark Office
Rh	average particle radius (as measured by dynamic light scattering)

I. INTRODUCTION

After months of needless delay, Plaintiffs began producing relevant laboratory notebooks from individuals involved in the development of the '542 patent shortly before the close of fact discovery. Their first such production included Notebook 670, which detailed certain experiments disclosed in the '542 patent and revealed that inequitable conduct was committed before the PTO.¹ As Plaintiffs concede (Opp. at 5, n.1), Novartis promptly moved to amend its pleadings to challenge the enforceability of the '542 patent due to inequitable conduct.

There is nothing “unusual” about Novartis’s inequitable conduct theory. *Id.* at 7. Two individuals involved in filing provisional applications to which the '542 patent asserts priority (John Fraser Wright and Gregory R. Bellomy) failed to disclose material information and took affirmative measures to hide its existence from the PTO. A third individual, the patent attorney who prosecuted the application that issued as the '542 patent (Roberta L. Robins), made affirmative misrepresentations of material facts that led directly to its issuance.

Plaintiffs oppose Novartis’s motion on the sole basis that its proposed amendment would be futile. But their contentions that Novartis’s allegations are “conclusory” are meritless, as the particularized factual bases for those allegations are detailed in over 137 paragraphs spanning 40 pages in Novartis’s proposed amended pleading (D.I. 239, Exhibit A). And the “scrutiny” applied by Plaintiffs in evaluating these allegations confirms their misunderstanding of the law. At base, Plaintiffs seek to litigate at the pleading stage whether the evidence to be adduced at trial is sufficient to establish inequitable conduct. That is improper. The appropriate inquiry is whether Novartis’s allegations fairly set forth circumstances which, if true and proven, support a finding of unenforceability. Novartis’s proposed amended pleading exceeds that bar.

¹ After Novartis sought the Court’s intervention (D.I. 242), Plaintiffs produced six additional lab notebooks on July 31, 2023, which Novartis is reviewing.

II. ARGUMENT

A. Novartis Adequately Alleged “But-For” Materiality

Plaintiffs argue that Novartis’s proposed pleading is futile because it has not “pled materiality with the specificity required by Rule 9(b).” Opp. at 1, 7-11. But Novartis has identified with particularity “what” misrepresentations and omissions were made as well as which claim limitations they were material to, “where” the misrepresentations and omitted information are located within materials of record, and “how” the Examiner would have reached a different conclusion regarding patentability with complete disclosure. That is all Rule 9(b) requires. *See Targus Int’l LLC v. Victorinox Swiss Army, Inc.*, C.A. No. 20-464-RGA, 2021 WL 2291978, at *5 (D. Del. June 4, 2021) (finding similar allegations sufficient under Rule 9(b)). And, as demonstrated below, Novartis’s factual allegations plausibly establish that the Examiner would have rejected the claims of the ’542 patent “but for” the material misrepresentations and omissions.

In response, Plaintiffs feign ignorance of applicable patent law and claim they have to “guess” how disclosure of the withheld information, particularly failed stability data for the 210 mM test formulation, would have prompted rejection at the PTO. Opp. at 8-9. That position is not credible. As detailed in Novartis’s proposed pleading, during prosecution of the application that issued as the ’542 patent, the claims were repeatedly rejected under 35 U.S.C. § 103. Am. Ans. at ¶¶ 167, 171. In response to these obviousness rejections, Ms. Robins (on behalf of the applicants) repeatedly pointed to Table 3 in the specification arguing that it supported non-obviousness based on alleged unexpected results. *Id.* at ¶¶ 169, 172. Specifically, she argued that Table 3 showed that “rAAV particles prepared and stored in elevated ionic strength solutions remain soluble and can be stored for an extended period.” *Id.* The Examiner maintained the obviousness rejection and took specific issue with this argument, noting that the alleged evidence of unexpected results was “not commensurate in scope with the degree of protection sought by the instant claims.” *Id.* at ¶ 173;

see *Invista N. Am. S.À.R.L. v. M&G USA Corp.*, No. 11-1007-SLR-CJB, 2013 WL 12304544, at *9 (D. Del. May 3, 2013) (citation omitted) (facts “indicating that the PTO was particularly concerned with a representation” sufficiently allege “but for” materiality). Whereas the claims were directed to compositions with an ionic strength of “greater than 200 mM,” Table 3 does not disclose any such composition with an ionic strength lower than 310 mM or greater than 510 mM. Am. Ans. at ¶¶ 127, 129, 157, 164, 209, 211. To address the Examiner’s concern, Ms. Robins revised her prior argument as follows: “[rAAV] particles prepared and stored in elevated ionic strength solutions (greater than 200 mM as claimed) remain soluble with no aggregation and can be stored for an extended period.” *Id.* at ¶¶ 137, 174 (emphasis added). This assertion was false. As Plaintiffs admit, the withheld data reports an Rh of [REDACTED] for the 210 mM test formulation after storage at [REDACTED] and an Rh of [REDACTED] for the 310 mM formulation after storage at [REDACTED] (Opp. at 12-14), and “[t]he specification notes that values above 20 nm indicate ‘the occurrence of *some level of aggregation*’” (*Id.* at 4 (emphasis added)).

Without access to the withheld stability data, the Examiner had no way of knowing that the statement was false. So “after consideration[] of” Ms. Robins’s revised argument, the Examiner allowed the claims with certain limited amendments. Am. Ans. at ¶¶ 176-82. Based on these facts, it is more than plausible that the Examiner would not have allowed the claims to issue had (1) Ms. Robins not made this material misstatement or (2) the Examiner possessed the undisclosed data demonstrating it was untruthful. In either case, the Examiner would have maintained the existing obviousness rejection, the details of which are readily ascertainable to Plaintiffs from the relevant PTO communications attached in Exhibit 3 to Novartis’s proposed pleading. *See* Fed. R. Civ. P. 10(c) (“A copy of a written instrument that is an exhibit to a pleading is part of the pleading for all purposes.”); *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 255 F.R.D. 443, 446 (W.D.

Mich. 2009) (“all purposes” includes satisfaction of Rule 9(b)). Plaintiffs’ inability to comprehend “how § 103 could apply at all given that the data at issue was confidential data generated by an inventor” (Opp. at 8-9) is disingenuous. Novartis does not contend that the withheld data itself renders the claims obvious—but rather that it disproves the argument made by Ms. Robins and credited by the Examiner in withdrawing an obviousness rejection based on the prior art.

This alone is sufficient to reject Plaintiffs’ argument that Novartis failed to adequately plead “but-for” materiality, as the claims of the ’542 patent would not have issued if the already-pending obviousness rejection was maintained. Nonetheless, Novartis also adequately alleges other grounds on which the Examiner would have rejected the claims but for the non-disclosure of material information. For example, if the Examiner knew that compositions having an ionic strength within the claimed range had been tested for their ability to prevent aggregation after various periods of “storage” and had failed, it is more than reasonable to infer that the Examiner would have rejected the claims under 35 U.S.C. § 112 for failure to describe or enable the full scope of claimed subject matter (Am. Ans. at ¶¶ 145, 216-20, 222-23, 229)—particularly, where Plaintiffs admit that the claims are “not limited to a particular timeframe of storage” (Opp. at 12, n.3). Further, caselaw Novartis cited in its pleading explains that, while a specification “must be taken as in compliance with the enabl[ement] requirement . . . unless there is reason to doubt the objective truth of the statements . . . which must be relied on for enabling support,” if “reason for such doubt does exist, a rejection for [lack of enablement] will be proper on that basis.” *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971); Am. Ans. at ¶ 144. Disclosure of failed stability data, including with a 210 mM formulation, would surely have given the Examiner reason to doubt the bald assertion in the specification that 200 mM is the “threshold ionic strength . . . required to prevent aggregation,” warranting an enablement rejection. *Id.* at ¶¶ 127, 163-64, 219, 222-23.

Separately, the '542 patent purports to teach that the extent of aggregation can be measured by filtering the composition through a 0.22 μm filter. *Id.* at ¶¶ 128, 191-93, 195-96, 232. That is the entire premise for claim 6 of the '542 patent, which requires that “recovery” of the rAAV particles in the composition be “at least about 90% following filtration.” *Id.* at ¶¶ 128, 240, 244. Referring to data in Table 2, the '542 patent states “[v]ector recovery (‘Yield %’) for both elevated ionic strength formulations . . . are significantly higher than the recovery using the control formulation,” which it attributes to “significant aggregation” with the control formulation. *Id.* at ¶ 243. However, additional data that was not disclosed to the PTO reveals that the true reason the reported “recovery” was lower for the control formulation is because there was less material being filtered—not based on pre-filtration aggregation. *See id.* at ¶¶ 231-45. If “recovery” had been reported based on the actual amount of material observed before filtration—[REDACTED] [REDACTED] (*id.* at ¶ 234)—as opposed to a theoretical target value, it would have shown no difference in “recovery” between the control formulation, which Plaintiffs contend does not prevent aggregation, and the higher ionic strength test formulations. *Id.* at ¶¶ 233-39, 242. Thus, disclosure of the actual data would have called into question the claimed method and caused the Examiner to reject at least claim 6 for lack of written description and enablement under § 112. Am. Ans. at ¶¶ 142-43, 242-45.

In sum, Novartis has adequately alleged “but for” materiality for the withheld information and false statements identified in its pleading. Plaintiffs’ cited cases do not compel a different conclusion. Their attempt to analogize to the decision in *Invista* underscores the adequacy of Novartis’s allegations, which, like those the *Invista* court found adequate, specifically “explain[] how the ‘undisclosed test results’ undercut an unexpected results argument which the ‘Examiner ultimately accepted.’” Opp. at 10, n.2 (citing *Invista*, 2013 WL 12304544, at *5, *9). The Court

“does not need to decide at this point” (i.e., the pleading stage) whether the withheld information and false statements identified by Novartis “are truly material.” *Targus*, 2021 WL 2291978, at *5.

B. Novartis Adequately Alleged “Intent to Deceive”

Plaintiffs also contend that Novartis “fails to satisfy the pleading requirement for the intent to deceive element.” Opp. at 16-18. But Plaintiffs misstate the law. Novartis need not “establish that the only reasonable inference from the record is intent to deceive.” *Id.* at 17. Instead, “that is a requirement to be met at the proof stage; at the pleading stage . . . a party must plead facts ‘from which the [c]ourt could reasonably infer that the patent applicant made a deliberate decision to deceive the PTO.’” *Invista*, 2013 WL 12304544, at *5. Novartis has satisfied this requirement.

Novartis’s allegations regarding Dr. Wright and Mr. Bellomy support a reasonable inference that each acted with the requisite intent to deceive the PTO. Specifically, Novartis has alleged that each “knew of withheld material information and withheld that information with the specific intent to deceive the PTO.” *Persawvere, Inc. v. Milwaukee Elec. Tool Corp.*, C.A. No. 21-400-GBW, 2023 WL 3750812, at *5 (D. Del. June 1, 2023). Dr. Wright’s awareness of the withheld information is readily apparent from the fact it was data from experiments he conducted prior to filing the ’997 Provisional. Am. Ans. at ¶¶ 130, 154-56, 159-61, 203-08, 235. His appreciation of the materiality is evidenced by, *inter alia*, his partial disclosure of certain details regarding the experiments in the same provisional application, which he authored. *Id.* at ¶¶ 136, 157-61, 183, 197-99, 228-29. Mr. Bellomy’s knowledge of the withheld information is reasonably inferred from the fact that a subsequent provisional application (the ’222 Provisional), which he prepared and signed, provided previously undisclosed experimental results that were only obtainable from the pages of Notebook 670 containing the withheld information. *Id.* at ¶¶ 132-33, 149, 162, 248. His appreciation of its materiality is reasonably inferred from his experience as a practicing patent attorney as well as the fact that the withheld information related to experiments

alleged to support patentability and included a failed 210 mM test formulation within the scope of the ionic strength limitation in the claims he filed. *Id.* at ¶¶ 135-36, 142, 145, 163-64, 246, 248-49, 251, 253-54. Moreover, the intent of Dr. Wright and Mr. Bellomy to deceive the PTO is reasonably inferred, for example, from their **removal** of references to that formulation and **renumbering** of test formulations to conceal its existence in the '222 Provisional to which each contributed, while simultaneously broadening the claims and disclosures to include that failed formulation. *Id.* at ¶¶ 157, 161-64, 200-201, 227, 231-32, 242-44, 250. Indeed, Dr. Wright confirmed he was involved in the decision to withhold information concerning this 210 mM formulation, which he described as not “compelling.” *Id.* at ¶ 200 (citing Ans. Ex. 2 at 315-328).

As for Ms. Robins, Novartis alleges that she made material misrepresentations during prosecution of the '542 patent. Ms. Robins made statements to the PTO that she knew were broad enough to encompass the failed 210 mM test formulation referenced in the '997 Provisional to which multiple applications she prosecuted, one of which issued as the '542 patent, asserted priority. *Id.* at ¶¶ 131, 134, 137-38, 140, 142, 148, 158, 165-66, 174, 246. It is reasonable to infer that Ms. Robins knew that the undisclosed experimental results for this formulation were unfavorable and contradicted the arguments she offered in support of patentability at least because (1) the '997 Provisional, which disclosed that the stability of the 210 mM had been tested, stated that higher ionic strengths of “preferably >300mM are required to substantially prevent aggregation”; and (2) when that statement was broadened in the '222 Provisional to assert “[a] threshold ionic strength of at least 200 mM is required to prevent vector particle aggregation,” all references to the 210 mM test formulation were removed. *Id.* at ¶¶ 135-36, 138, 140, 142, 145, 158, 161-63, 228-29, 253-54. Further, even if one were to assume that Ms. Robins did not know of the contradictory data, she plausibly knew of the experiment (*id.* at ¶¶ 131, 202), and it is reasonable

to infer a specific intent to deceive if her express representation to the PTO was made without sufficient knowledge. *See 3D Med. Imaging Sys., LLC v. Visage Imaging, Inc.*, 228 F. Supp. 3d 1331, 1338-39 (N.D. Ga. 2017) (granting summary judgment of inequitable conduct based on patent attorney's express representation about a fact he admitted having no knowledge about).

Plaintiffs' argument that "Novartis has failed to allege any specific factual allegations separate from its materiality assertions that would support an inference of intent to deceive" (Opp. at 17) is incorrect.² Novartis's allegations identify affirmative actions taken by the identified individuals, with full appreciation of their materiality and misleading nature, permitting a reasonable inference those actions were intended to deceive the PTO.

C. Plaintiffs' Interpretation of the Data Cannot Establish Futility

Plaintiffs devote pages of their opposition to quibbling about whether certain of the undisclosed data actually supports Novartis's positions. Opp. at 11-16. But these arguments invariably do not accept Novartis's allegations as true or view them in the light most favorable to Novartis—as required in assessing futility. *See Targus*, 2021 WL 2291978, at *3-4 (citations omitted) (discussing futility analysis). As such, the Court need not entertain Plaintiffs' arguments to resolve this motion. Nevertheless, those arguments lack merit, as set forth below.

Plaintiffs' attempts to reconcile the withheld stability data for the 210 mM test formulation with Ms. Robins's material misstatement are belied by the record and, in any case, cannot excuse withholding that data from the PTO. Plaintiffs first suggest that the term "extended period" used by Ms. Robins during prosecution "refer[s] to the five-day data in Table 3 of the specification." Opp. at 12. But they ignore that the statement was made in the context of an argument that the

² Notwithstanding Plaintiffs' related complaints (Opp. at 8), allegations "upon information and belief" are permitted under Rule 9(b) when "essential information lies uniquely within another party's control" as long as "the pleading sets forth the specific facts upon which the belief is reasonably based." *Exergen Corp. v. Wal-Mart Stores, Inc.*, 575 F.3d 1312, 1330 (Fed. Cir. 2009).

claimed compositions are “commercially viable” (Am. Ans. at ¶¶ 169-174), rendering it entirely plausible that Ms. Robins meant, and the Examiner understood, something longer than five days as would be relevant for commercial application. Indeed, the inventors each confirmed commercial development of an AAV composition requires stability over one or more years of storage. Ex. 24 at 135:16-23, 149:1-12; Ex. 25 at 141:11-143:17. And, although the term “extended period” appears only twice in the specification, in each instance it was used to refer to a period significantly longer than five days. Ans. Ex. 1 at 9:60-10:7 (referring to 45-day study assessing the impact of preparation and storage on AAV functional activity), 10:40-43 (same). But even if “extended period” was interpreted to mean five days, the undisclosed 210 mM test formulation did not effectively prevent aggregation at that time point. In fact, the data in Notebook 670 indicates that

210 mM formulation

(Opp. at 11; Am. Ans. at ¶¶ 218-19),

(see Opp. at 4 (citing Ans. Ex. 1 at 9:19-54)).

Plaintiffs next contradict themselves by asserting that the [REDACTED] for the 210 mM formulation [REDACTED] that it prevented aggregation because the claims are “not limited to a particular timeframe of storage.” Opp. at 12, n.3. But if the six-day data were considered relevant for this reason, so too would the [REDACTED] [REDACTED]

Am. Ans. at ¶¶ 218-19. Likewise for the [REDACTED] for the 310 mM formulation, which indicates that formulation did not prevent aggregation [REDACTED] [REDACTED]. *Id.* at ¶¶ 218, 220. All in all, not only does the stability data disprove Ms. Robins’s assertion during prosecution that the rAAV particles “remain soluble with no aggregation and can be stored for an extended period,” it shows sufficient day-to-day variance to question whether it is

reliable to support **any** conclusion about the ability of the compositions to prevent aggregation.

Plaintiffs' argument that most (not all) of the undisclosed stability data for [REDACTED] [REDACTED].
Opp. at 13-14. Plaintiffs concede that the data for the 310 mM formulation [REDACTED] [REDACTED]. *Id.* at 4, 14. Novartis alleges that the selection by Dr. Wright and Mr. Bellomy of five days as the timepoint for the data included in Table 3, which concealed data showing the 310 mM formulation [REDACTED] [REDACTED], was intended to deceive the PTO into believing both formulations worked as intended—[REDACTED]. Am. Ans. at ¶¶ 220, 227.

Finally, Plaintiffs' argument that the undisclosed data regarding the filtration experiment in Table 2 “still supports claim 6” because “the formulations with an ionic strength greater than 200 mM still [REDACTED] [REDACTED]” (Opp. at 14-16) also misses the point—there is no evidence that the “at least about 90%” threshold for recovery following filtration recited in claim 6 constitutes a reliable method of assessing significant aggregation.³ That is contrary to what the applicants, specifically Dr. Wright and Mr. Bellomy, told the PTO in the specification of the '222 Provisional Application they jointly prepared, which was incorporated in relevant part without modification in the application that issued as the '542 patent. *E.g.*, Am. Ans. at ¶¶ 232-237, 242-45.

III. CONCLUSION

For the foregoing reasons, Novartis respectfully requests that the Court grant its motion.

³ Plaintiffs also discuss a third experiment depicted in Fig. 1B. Opp. at 2. But that experiment is irrelevant and could not support the claims of the '542 patent, at least because the compositions did not have the claimed concentration of vector particles and were not stored prior to being tested for aggregation. *See, e.g.*, Ex. 24 at 203:17-24 (the concentrations were at most 1×10^{13} vg/mL prior to dilution); Ans. Ex. 1 at 12:45-46 (“data collection is initiated within 10 seconds of mixing”).

Dated: August 4, 2023

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Exhibit 24



Highly Confidential

Transcript of John Fraser Wright

Date: June 16, 2023

Case: Genzyme Corporation, et al. -v- Novartis Gene Therapies, Inc., et al.

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Transcript of John Fraser Wright
Conducted on June 16, 2023

1 (1 to 4)

1 1 IN THE UNITED STATES DISTRICT COURT 2 FOR THE DISTRICT OF DELAWARE 3 4 -----X 5 GENZYME CORPORATION and : 6 AVENTIS INC., : 7 Plaintiffs, : 8 vs. : C.A. No. 9 NOVARTIS GENE THERAPIES, INC. : 21-1736 (RGA) 10 and NOVARTIS PHARMACEUTICALS : 11 CORPORATION, : 12 Defendants. : 13 ----- X 14 15 HIGHLY CONFIDENTIAL 16 VIDEOTAPED DEPOSITION OF JOHN FRASER WRIGHT 17 Palo Alto, California 18 Friday, June 16, 2023 19 9:30 A.M. 20 21 22 23 Job No.: 496641 24 Pages: 1-379 25 Reported by: Crystal Hereford, RPR 2	3 1 A P P E A R A N C E S 2 3 ON BEHALF OF PLAINTIFFS: 4 AMANDA K. ANTONS, Ph.D. 5 DECHERT, LLP 6 35 West Wacker Drive, Suite 3400 7 Chicago, Illinois 60601 8 312.646.5800 9 and 10 JONATHAN D.J. LOEB, Ph.D. 11 DECHERT, LLP 12 3000 El Camino Real 13 Five Palo Alto Square, Suite 650 14 Palo Alto, California 94306 15 650.813.4800 16 17 18 19 20 21 22 23 24 25
1 Videotaped deposition of JOHN FRASER 2 WRIGHT, conducted at the law offices of 3 DECHERT, LLC, 3000 El Camino Real, Five Palo Alto 4 Square, Suite 650, Palo Alto, California 94306. 5 6 7 8 Pursuant to notice, before 9 CRYSTAL HEREFORD, Registered Professional Reporter, 10 Certificate No. 30819; California Certified 11 Reporter, Certificate No. 14416; and Arizona 12 Certified Shorthand Reporter, Certificate No. 50893. 13 14 15 16 17 18 19 20 21 22 23 24 25 2	4 1 A P P E A R A N C E S 2 3 ON BEHALF OF DEFENDANTS: 4 M. DAVID WEINGARTEN, Ph.D. 5 FINNEGAN, HENDERSON, FARABOW, 6 GARRETT & DUNNER LLP 7 217 17th Street, NW, Suite 1400 8 Atlanta, Georgia 30363 9 404.653.6449 10 and 11 CHRISTOPHER W. WEBER, Ph.D. 12 FINNEGAN, HENDERSON, FARABOW, 13 GARRETT & DUNNER LLP 14 901 New York Avenue, NW 15 Washington, DC 20001 16 202.408.4000 17 18 ALSO PRESENT: 19 JOE RAMIREZ, Video Specialist, Planet Depos 20 21 22 23 24 25 4

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Sarepta, Exhibit 1086, page 19

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Transcript of John Fraser Wright

2 (5 to 8)

Conducted on June 16, 2023

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3 (9 to 12)

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9 1 PROCEEDINGS 2 THE VIDEOGRAPHER: Here begins Media 3 Number 1 in the videotaped deposition of Dr. John 4 Fraser Wright in the matter of Genzyme Corporation, 5 et al., versus Novartis Gene Therapies, Inc., 6 et al., in the United States District Court, for the 7 District of Delaware, Case Number 21-1736 (RGA). 8 Today's date is June 16, 2023. The time 9 on the video monitor is 9:30 a.m. Pacific Standard 10 time. 11 The videographer today is Joe Ramirez, 12 representing Planet Depos. 13 This video deposition is taking place at 14 Dechert LLP, Palo Alto. 15 Would counsel please voice-identify 16 themselves and state whom they represent. 17 MR. WEINGARTEN: David Weingarten from 18 Finnegan, Henderson, Farabow, Garrett & Dunner, 19 representing Defendant Novartis entities, and joined 20 with me today is Christopher Weber, also of 21 Finnegan. 22 MS. ANTONS: Amanda Antons of Dechert LLP, 23 representing Plaintiffs and the witness. 24 THE VIDEOGRAPHER: The court reporter 25 today is Crystal Hereford, representing	11 1 over the rules probably in a little bit more detail. 2 A. Thank you. 3 Q. But I think the key issue here is, is that 4 I'm going to ask you some questions. You're going 5 to answer those questions under oath. 6 We have a court reporter here that's going 7 to take down what you say. 8 A. Uh-huh. 9 Q. If you don't understand the question that 10 I ask, then just ask for clarity. You know, I can 11 repeat the question or I can rephrase the question. 12 A. Uh-huh. 13 Q. If you answer the question, I'm going to 14 assume you understood it. 15 A. Uh-huh. 16 Q. When I ask you a question, your counsel 17 might object. 18 A. Uh-huh. 19 Q. If she objects, unless she instructs you 20 specifically not to answer it, you still have to 21 answer it. We'll deal with the objections later. 22 A. Uh-huh. 23 Q. With regard to the questions that are 24 being asked, there are going to be a number of 25 questions being asked, and there might be a point in
10 1 Planet Depos. 2 The witness will now be sworn. 3 JOHN FRASER WRIGHT, 4 a witness herein, having been first duly sworn by 5 the certified reporter to speak the truth and 6 nothing but the truth, was examined and testified as 7 follows: 8 EXAMINATION 9 BY MR. WEINGARTEN: 10 Q. Good morning. 11 A. Good morning. 12 Q. Could you please state your full name for 13 the record? 14 A. John Fraser Wright. 15 Q. And where do you currently reside, 16 Dr. Wright? 17 A. I reside at [REDACTED] 18 [REDACTED]. 19 Q. And, Dr. Wright, you understand that 20 you're being deposed here today? 21 A. Yes. 22 Q. And we're going to go over some ground 23 rules. Have you been deposed before? 24 A. No. 25 Q. So the first time deposed, so we'll go	12 1 time that, you know, I lose track of time, and you 2 might need to take a break -- 3 A. Yeah. 4 Q. -- for whatever reason. Or counsel might 5 ask for a break as well. And we'll certainly 6 accommodate you. 7 But if we're in the middle of a question 8 or if we're in the middle of a series of questions 9 related to a document, we might ask you to just wait 10 a few minutes, but we will be mindful of the break, 11 and we'll certainly give it to you. 12 A. Could I ask for a clarification? 13 So a series of questions. So that would 14 be within a few minutes. Is that correct? 15 Q. Well, presumably it would be. But, 16 you know, I guess the short answer is, is that if 17 you ask for a break, I'll do my best to give it to 18 you right away. 19 A. Okay. Thank you. 20 Q. No problem. 21 And, you know, when I ask you questions, 22 the court reporter is trying to jot down or put down 23 what you've said and also what I've said. 24 A. Uh-huh. 25 Q. I tend to speak quickly, so she might have

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4 (13 to 16)

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13 1 to tell me a number of times to slow down. And she 2 might do the same for you. I don't know. 3 But ultimately, when you answer the 4 question, she's unable to really put down the "ums" 5 and "yeah" and shaking of heads. So try the best 6 you can to provide verbal answers, you know, such as 7 "yes," "no," whatever the answer is to the question 8 rather than motions and so forth. 9 A. Sure. Understood. Uh-huh. 10 Q. Is there any reason that you're unable to 11 provide, you know, honest and truthful testimony 12 here today? 13 A. No. There's no reason. I'm not sure if 14 it'll come to this, but I would just like to state 15 that I'm -- you know, I'm 65. And, you know, I wear 16 bifocal glasses, and, you know, these days I quite 17 often ask "Can you repeat the question?" when I'm 18 speaking with my family. So just understand that I 19 have probably what's typical somewhat reduced 20 hearing and vision at this stage. 21 Q. I appreciate that. I can understand that 22 and have similar issues myself. So I will do my 23 best to be mindful. 24 A. Thank you. 25 Q. But if you need time to review something,	15 1 Do you see that? 2 A. I do. Yes. 3 Q. Okay. And do you see right underneath 4 that, it refers to the defendant's notice of 5 deposition of John Fraser Wright? Do you see that? 6 A. I do. Yes. 7 Q. And take a second to look at the 8 document -- it's only a few pages -- and tell me if 9 you've seen this document before. 10 A. Yes. I have seen the document, and I've 11 looked at the three pages. This is a document that 12 I am familiar with. Yes. Uh-huh. 13 Q. All right. And so you understand that 14 you're here to provide your testimony in your 15 personal capacity and to answer the questions the 16 best you can remember? 17 A. Uh-huh. Yes. Uh-huh. Yep. 18 Q. What did you do prepare for your 19 deposition today, Dr. Wright? 20 MS. ANTONS: I'll just caution the witness 21 to not disclose conversations with counsel. You can 22 answer questions generally. 23 THE WITNESS: Okay. So specifics of 24 conversations. 25 MS. ANTONS: Yes. Our conversations are
14 1 you know, take your time. We're not under a rush 2 here. We have the day. We certainly will do what 3 it takes to make sure that you have the ability to, 4 you know, review whatever is in front of you. 5 A. Thank you. I appreciate it. Uh-huh. 6 Q. Now, you said this is the first time 7 you're being deposed. How did you learn that you 8 were going to be deposed? 9 A. I learned from a reach-out from Dechert, I 10 believe, or the preceding legal firm. Another point 11 is I'm not great with name recollection, especially 12 in the area that I'm not familiar with. And I think 13 the deposition information came about a month or six 14 weeks ago, something like that. 15 MR. WEINGARTEN: So I'm going to ask the 16 court reporter to mark this as -- I guess we'll go 17 with Wright Exhibit 1. 18 (Exhibit Number 1 marked.) 19 A. Great. 20 Q. And, Dr. Wright, what's been handed to you 21 has been now marked as Wright Exhibit 1. 22 A. Uh-huh. 23 Q. And it has at the top the -- what we'll 24 refer to as the case caption, Genzyme Corporation 25 and Aventis v. the Novartis Gene Therapy entities.	16 1 privileged, so you cannot share -- disclose what we 2 spoke about. 3 THE WITNESS: I understand. Yeah. 4 A. So I have met with Dechert counsel in 5 preparation yesterday, for example, for much of the 6 day. That's the primary preparation. 7 I have also reviewed, myself, relevant 8 documents. I have relevant publications, at least a 9 couple, you know, in the peer-reviewed literature. 10 And I've had a copy of the patent, of 11 course. 12 And most recently, I've been able to view 13 some additional documents, including lab notebooks 14 from that time and also a provisional patent version 15 that was prepared in 2004. 16 Q. So let's just -- the first thing you said 17 was that you met with Dechert yesterday. Could 18 you -- without going into specifics, do you 19 recall -- I know you said you're not good with 20 names, but do you recall who you met with? 21 A. Amanda. 22 Q. Was there anybody else present during that 23 time? 24 A. Yes. 25 Q. And who was present?

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133 1 A. Yes. 2 Q. [REDACTED] 3 [REDACTED] 4 [REDACTED] 5 [REDACTED] 6 A. Uh-huh. Uh-huh. 7 Q. Do you see that? 8 A. Yes. Uh-huh. 9 Q. [REDACTED] 10 [REDACTED] 11 [REDACTED] 12 [REDACTED] 13 A. Uh-huh. 14 Q. Did I read that right? 15 A. Yes. 16 Q. [REDACTED] 17 [REDACTED] 18 A. Okay. 19 Q. [REDACTED] 20 [REDACTED] 21 [REDACTED] 22 And what's the purpose of the rigorous QC 23 testing out to five years? 24 A. To establish stability, so -- yeah, to 25 establish long-term stability -- reasonably	135 1 material that's stored in the freezer, or however 2 you have it stored, as you're moving forward in the 3 clinical development. If you're doing, let's say, 4 every three months, as long as your last data point 5 was okay, then you can claim that you still have 6 stability. I think that's generally deemed 7 acceptable by the FDA for -- phase clinical -- 8 Q. So it's -- what if you only have seven 9 days' stability? Is that sufficient for QC rigorous 10 testing? 11 MS. ANTONS: Objection; form. 12 A. It's a different context. Seven days on 13 a -- on a clinical lot would be good for 14 administration to the seventh day for a subject. 15 Yes. Uh-huh. 16 Q. And what about for commercial purposes? 17 A. Commercial purposes, typically you have 18 completed all of the stability studies during 19 clinical development. Then you simply aggregate the 20 data and provide an expiry date, which might be 21 three years, five years, ten years, depending on the 22 storage conditions. Or shorter. It could be 23 shorter or longer. 24 Q. And for, let's say -- you said three years 25 as an example.
134 1 long-term stability. 2 Q. And what makes five years reasonable? 3 A. Well, I think if you imagine that was -- 4 one was -- if a sponsor invested money to the point 5 where they could produce a GMP lot to support Phase 6 I/II clinical studies. And for something like AAV 7 vectors, that's not a trivial endeavor. It may cost 8 a million dollars, it may cost \$5 million, may cost 9 \$10 million, you know, in today's dollars. 10 So you can imagine that a clinical study 11 could take years to perform. So the concept that 12 you start -- and, of course, it's very important 13 that in a clinical study, if you administer vector 14 to, say, nine subjects over the course of three 15 years -- let's say it takes that long for whatever 16 reason. It's not too rare of a phenomenon, frankly, 17 in AAV gene therapy because of all the complexities. 18 Then you have to have an assurance that 19 the material that you gave to the Patient Number 1 20 one month after that lot had been prepared is really 21 the same as the material that you gave to Patient 22 Number 9, let's say, three years later. And hence, 23 you have to do -- typically it's acceptable for 24 Phase I clinical studies to do concurrent stability, 25 and that means that you'd be monitoring your	136 1 A. Uh-huh. 2 Q. For a three-year expiry date, what kind of 3 stability would you need? 4 A. For a three-year expiry date, you'd need 5 to demonstrate acceptable consistency of what would 6 be called critical quality attributes related to 7 safety, purity, and potency and identity of the 8 product right out through three years and probably 9 plus. I think there'd probably be an expectation of 10 a longer time frame. It might be 150 percent. 11 You know, again, I'm not a 12 commercial-level person, and there are real 13 considerations that, you know, big players would 14 know. You don't want your material to expire just 15 the day after its last use. I mean, just like milk 16 that we have in the fridge, right? 17 Q. You can put that aside. 18 MR. WEINGARTEN: If you could please mark 19 that as Wright Exhibit 8. 20 (Exhibit Number 8 marked.) 21 THE REPORTER: It's marked on the back. 22 THE WITNESS: It's marked on the back. 23 Okay. 24 Q. Doctor, you have before you what's been 25 marked as Wright Exhibit 8. Do you see that?

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145 1 Q. Jurg Sommer. Sorry. 2 A. Uh-huh. 3 Q. And both of them, if I recall, worked in 4 the group that you referred to as -- they were 5 scientists that worked as -- reporting to you in one 6 way or the other? 7 A. Yeah. Chunlin Tang, I suspect, was a 8 senior scientist, formulation. And Jurg Sommer was 9 an assistant or an associate director or a director 10 in charge of analytical methods development. 11 Uh-huh. 12 Q. And these two individuals are being lab 13 scientists. 14 A. Jurg was at a management level. He was a 15 director level. I don't think he'd describe himself 16 as a lab scientist. He might have been in 17 sometimes. 18 Chunlin was a lab scientist. Yes. 19 Q. And out of all the people listed here -- 20 A. Uh-huh. 21 Q. -- Chunlin Tang is the only lab scientist 22 that's listed here. 23 A. Yeah. But as I mentioned to you before, 24 that, you know, in such a small environment, the 25 directors are also in the lab sometimes. And I	147 1 MS. ANTONS: Objection; form. 2 A. Yeah. I think, in general, of all the 3 viruses that you consider, there are two flavors, if 4 I could do it that way, in a slightly lay version 5 there. One division is that there's a structure 6 that is called non-enveloped. So the outside of the 7 virus is just a protein. It's capsid protein or 8 something. And enveloped viruses have this lipid 9 bilayer around them, like our own cells do. So 10 there's quite a distinction between these two 11 categories in terms of their behavior. 12 Q. And if you look on page 173 of what I 13 believe is marked as Wright Exhibit 9. 14 A. 9. So that's -- 15 Q. Yes. 16 A. -- the one that I'm sitting on. 17 173 -- I see. Starting with 174, yeah. 18 Uh-huh. So that's page 174 that I see. 19 Q. That's right, page -- sorry -- page 1 -- 20 let me scratch that. I'll start over and make it 21 clear. 22 A. Uh-huh. 23 Q. If you could go to Wright Exhibit 9, the 24 first page. 25 A. Yes.
146 1 think that applied across the board here, certainly 2 for Guang and I, especially for Guang. Yeah. 3 Q. And Chunlin Tang being a scientist, would 4 he have had a lab notebook? 5 A. He should have. Uh-huh. Uh-huh. 6 Q. And what about Jurg Sommer? 7 A. I don't know. I'm not sure if he'd have a 8 lab notebook assigned to him. Uh-huh. He may have 9 had the discretion. I think there would be "I need 10 a lab book -- notebook because I'm going to do some 11 experiments." 12 You know, and then we'd say, "Well, let's 13 go get one issued." Right. Uh-huh. 14 Q. Now, you mentioned earlier today -- when 15 we were discussing some of the prior work that you 16 had done, prior to Avigen -- 17 A. Yes. 18 Q. -- you had mentioned the phrase 19 "enveloping viruses." 20 A. Enveloped. 21 Q. Enveloped virus. 22 A. Yeah. Uh-huh. Uh-huh. 23 Q. It sort of begs the question to me: That 24 means there's non-enveloped viruses? 25 A. Yeah.	148 1 Q. The right-hand column. 2 A. Yes. 3 Q. And you go down to the last full paragraph 4 that begins "Formulation development." Do you see 5 that? 6 A. Yes. 7 Q. And you see in the middle of the 8 paragraph, approximately seven or eight lines down, 9 it says "Because AAV and adenoviruses are both 10 non-enveloped viruses developed as gene transfer 11 vectors, studies on the latter can provide guidance 12 for AAV vector formulation development." 13 And you go on to say, further down in 14 that -- first of all, before I do that -- 15 A. Uh-huh. 16 Q. -- you agree that's what you wrote, right? 17 A. Well, it's written there, and I'm the 18 first author in this paper. Yes. 19 Q. And if you go down further on that page, 20 it says -- this is the second-to-the-last line. 21 A. Uh-huh. 22 Q. "Extended storage periods is a major 23 challenge in the formulation development of AAV 24 vectors." 25 A. Yes. That's what it says.

149 1 Q. And then it goes on to say "Formulations 2 and storage conditions must be amenable to 3 commercial development of a biological product." Do 4 you see that? 5 A. Yes. Uh-huh. That's -- 6 Q. Did I read that right? 7 A. Yes, you did. Yes. 8 Q. And that's what we were talking about a 9 little bit ago about the commercial development 10 stability. I think you said three years would be 11 not unreasonable. 12 A. Yeah, for example. Uh-huh. Uh-huh. 13 For clarity, there may be products that 14 are stored in the deep freeze that, in principle, 15 could be stable for ten years. And in principle, 16 there may be products that are very unstable and 17 they can't be frozen and they may have to be used 18 within months. So there's a broad range. It really 19 depends. There's quite a heterogeneity. 20 Q. So storage, in your mind, could be frozen 21 or non-frozen, depending upon the application? 22 MS. ANTONS: Objection; form. 23 Q. You can answer. 24 A. Yes. 25 Q. And if go on to the next full paragraph,	151 1 DNA, RNA, whatever it might be, and proteins. So a 2 cryoprotectant is something that somehow mitigates, 3 at the very least, some of the stresses that may be 4 induced during the freeze-thaw process. 5 Q. And so you used the word "freeze-thaw 6 process." 7 A. Uh-huh. 8 Q. So I want to make sure I understand this. 9 You said these things could be stored frozen. 10 A. Yes. 11 Q. But you don't use them frozen? 12 A. No. 13 Q. So you have to thaw them. 14 A. Yes. 15 Q. So when you refer to a freeze-thaw 16 process, it's the process of storing and frozen and 17 then thawing when you're ready to use? 18 A. As the first irreducible instance, yes. 19 And there may be other reasons that a freeze-thaw 20 may be introduced, perhaps taking a sample, perhaps 21 as part of the manufacturing process. So hence, 22 there is an interest in understanding multiple 23 freeze-thaw characteristics. 24 But one is -- if it's a frozen product, 25 one would be the minimal amount, the frozen-thaw.
150 1 the next section, this is a section titled "Vector 2 Formulation Development for Optimal Stability During 3 Purification and Storage." "Storage Temperature" is 4 the subheading underneath that. Do you see that? 5 A. Yes. 6 Q. And the first sentence says "AAV vectors 7 are typically formulated and stored in 8 neutral-buffered saline solution." 9 A. Uh-huh. 10 Q. And the next sentence says "In some cases, 11 a cryoprotectant, glycerol or sorbitol," as 12 examples, "is added to preserve vector activity 13 following storage at negative 20 or negative 80 14 degrees C." 15 A. Right. Uh-huh. 16 Q. What's a cryoprotectant? 17 A. Well, I mean, a cryoprotectant is some 18 type of excipient that can preserve the critical 19 quality attributes of, for example, a product like 20 an AAV vector. But this applies to anything, any 21 product that might be -- let's say, a human product 22 for injection -- anything like that. 23 And so there are stresses induced during 24 the freeze process that can affect the stability of 25 certain molecules, be they viruses, viral vectors,	152 1 You can't administer a frozen product into the back 2 of the eye or the brain or into the blood of people. 3 Q. So following storage, you defrost it or 4 thaw it. 5 A. Yes. 6 Q. And then you use it. 7 A. Yeah. And you probably warm it to the 8 appropriate temperature. It depends on the 9 procedures. Uh-huh. 10 Q. And stability during that period of time 11 is important? 12 A. Very important, of course. 13 Q. You can put that one down. 14 A. Thank you. 15 Can I just make an additional comment? If 16 I could, I want to expand on the -- so the 17 preparation of a product to administer into a human 18 subject involves, as we've discussed, if it had been 19 frozen, thawing it and then manipulating it. And 20 that manipulation would typically occur perhaps at 21 4 degrees, perhaps at room temperature for -- so 22 over the course of those hours, it's very important 23 to have an assurance that the product that you're 24 injecting into the person ultimately has retained 25 the characteristics that you tested when you

197 1 Q. And in that approach that you're referring 2 to, is that an approach which will also observe 3 aggregation if it occurred? 4 A. It would, but there's a very significant 5 limitation. 6 Q. Okay. And what's that limitation? 7 A. The limitation is -- a clear benefit and 8 advantage of the DLS is the very, very high 9 sensitivity of the readout and the very, very low 10 input that is required. Doing something like pure 11 spectrophotometry and the OD, optical density, 12 measurements that I measured would have required 13 logs more vector, perhaps tenfold, perhaps 14 hundredfold. And, in fact, these vectors are hard 15 to make and hard to -- you know, when you're doing a 16 hundred different conditions, you can't really do it 17 that way. 18 Q. So the problem is getting enough material 19 to do it? 20 A. Yeah. Yeah. 21 Q. And with regard to your dynamic light 22 scattering -- in fact, let's go ahead and look at 23 that for a minute. 24 A. Uh-huh. 25 Q. If you go to Column 4 of the patent --	199 1 Q. Do you see that? 2 A. Yes. 3 Q. What's meant by "vector dilution?" 4 A. So this is a core feature of this 5 important screening assay that is generally 6 presented in Figure 1. The concept is that you take 7 a small amount -- a small volume of vector that is 8 stable in a formulation that we feel was going to 9 retain stability, and we prove it by just watching 10 it over time by itself -- and diluting 80 percent 11 volume of something else. 12 So as an example, if you put 80 percent 13 water, all of a sudden, you go from something that 14 is stable to something that is no longer stable and 15 aggregates. So water is the most extreme way of 16 reducing the ionic strength. 17 Q. So when you say "diluting," you're 18 diluting the concentration of the vector. 19 A. You are. Yes. You are diluting the 20 concentration of the vector. You're diluting 21 everything in that original -- be it 22 20 microliters -- I can't remember the volumes, but 23 it was like 80 microliters added to 20 microliters, 24 or whatever the volume of that Q-vat (phonetic) was, 25 the same proportion.
198 1 this is Wright Exhibit 11. 2 A. Uh-huh. 3 Q. -- and you look right under -- it says 4 "Description of the Drawings," and it refers to 5 Figures 1A and 1B. Do you see? 6 A. Yes. Line 14. Uh-huh. 7 Q. And go ahead and read that paragraph to 8 yourself. 9 A. Uh-huh. 10 Okay. I've read that paragraph. 11 Q. Okay. Now, it refers to determining 12 the -- scratch that. 13 It refers to AAV2-FIX vectors prepared by 14 what refer -- what it refers to as Method 2 of 15 Example 1. 16 A. Uh-huh. 17 Q. And it says "Average particle radius is 18 measured by dynamic light scattering, DLS, followed 19 by vector dilution in various concentration of 20 excipients." 21 A. "Following" -- 22 Q. "Following," yes. 23 A. -- "vector dilution." Yeah. Uh-huh. 24 Q. Following. 25 A. Uh-huh.	200 1 Q. So you say that you "take a small volume 2 of vector that is stable in a formulation that we 3 feel was going to retain stability, and we prove it 4 by just watching it over time by itself." 5 A. That's correct. Uh-huh. As one arm of a 6 series of samples that might include 10 or 7 20 different samples. That would be one of the 8 control samples. 9 Q. My eyes are not what they used to be. 10 Give me -- 11 A. Me too. Me too. 12 Q. -- a minute here. I should have gotten my 13 glasses out. I don't want to interrupt things now, 14 though. 15 A. It's okay. 16 Q. And so, Doctor, let's turn to Column 12. 17 A. Okay. 18 Q. And line 40. 19 A. Yes. 20 Q. And that refers to a "dilution-stress 21 method." Do you see that? 22 It say "A 'dilution-stress' method is used 23 to assess the effect of varying excipients on vector 24 aggregation." Do you see that? 25 A. Yes. Uh-huh.

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201 1 Q. And that -- and you have a good memory. 2 Because that says "In this method, 80 3 microliters" -- 4 A. Yep. 5 Q. -- "of a test diluent is added to 6 20 microliters of vector with mixing." Do you see 7 that? 8 A. Yes. 9 Q. And that's the experiment that is being 10 referred to in Figures 1A and 1B. Is that right? 11 A. Yes. That was that screening experiment. 12 Yes. Uh-huh. 13 Q. And that screening experiment, according 14 to this, was done within ten seconds, right? 15 A. So done within -- within ten seconds of 16 mixing. So let me refresh. 17 Initiated. It was initiated. So the data 18 collection was initiated within ten seconds. 19 You have to understand that to perform the 20 dilution -- we didn't have robotics. So, for 21 example, me, I would have a pipette in there, and 22 I'd put that 80 microliters of the diluent or -- 23 you know, and I'd typically repipette it two or 24 three times. So -- and then you have to close the 25 machine, and then you start data collection. So,	203 1 formulations -- 2 A. Uh-huh. 3 Q. -- there was precipitation before you even 4 started. 5 A. No. That would be controlled for in the 6 experiment. So we would start with material that 7 would read clean without any aggregation at the 8 beginning -- at the beginning, at point-zero, before 9 the dilution happened. Aggregation may start very 10 quickly, but it's still going to be within tens of 11 minutes -- tens of seconds to minutes. 12 Q. But if it wasn't clean at the beginning, 13 you would filter it to remove the stuff that -- 14 A. That is true. 15 Q. And then you would test it. 16 A. That's true. 17 Q. And what's the concentration of those 18 samples that you filter? 19 A. It would be a fixed concentration that 20 would give a good readout on the machine. So I 21 can't recall specifically. It would be something -- 22 I suspect something like 1E13 or 5E12. These are 23 general stock. It would be a stock factor 24 preparation. 25 Q. So whatever the concentration is at the
202 1 you know, within ten seconds. 2 Q. Within ten seconds of start. It could be 3 five. It could be ten. 4 A. Yeah. Yeah. Yeah. 5 Q. And you're getting a result. 6 A. Yes. 7 Q. And that's the result that's reported in 8 the figures. 9 A. Well, the figures report a secondary 10 calculation. So if you go back to the notebook, 11 you'll see that really what happens is you -- when 12 vector aggregates as a function of time, you have 13 the series of curves. And there are dozens of 14 figures in the notebooks as we evolved our 15 information. The same data, though. It's secondary 16 evaluation of that primary data. 17 Q. Well, the primary data is data obtained 18 from the DLS within ten seconds of mixing it. 19 A. No, starting from -- starting from ten 20 seconds and probably going for some minutes. So -- 21 Q. So it may take a couple of minutes to -- 22 A. It may take a couple of minutes. You'd 23 have to look at the graphs. But this all happens 24 within minutes in the readout. Yes. Uh-huh. 25 Q. And in this experiment, in some of those	204 1 beginning -- 2 A. Yeah. 3 Q. -- in some formulations, you would dilute 4 it 1-to-4 -- 5 A. Uh-huh. 6 Q. -- and then test it? 7 A. And watch -- kinetically watch over the 8 course of time the formation of -- if it occurred, 9 the evolution of the average radius measured. 10 Q. Over those two minutes or so. 11 A. Yeah. Let's call it two -- it might be 12 five. You'd just look at the X axis in the -- 13 Q. I'm not going to hold you to two minutes. 14 A. Okay. Thank you. Okay. 15 Q. But in some instances -- 16 A. Uh-huh. 17 Q. -- there's precipitation before you begin, 18 so you dilute -- I mean, you filter through a 19 filter, and then you do the test. 20 A. Oh, before you begin. Yeah. So you don't 21 do the test -- it would not make sense to do the 22 test with material that already has some evidence of 23 aggregation. That's right. So before you even 24 start the procedure, you would verify that the -- 25 your -- because this is -- you have to start from

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Transcript of John Fraser Wright

95 (377 to 380)

Conducted on June 16, 2023

377 1 A. Yes, I have it. 2 Q. Okay. And do you recall earlier when 3 counsel was asking about the Test Formulation 2 in 4 Exhibit 17 that was not included in the '542 patent? 5 A. Yes, I do. 6 Q. Okay. And Test Formulation 2 in 7 Exhibit 17 contains glycerol. Is that right? 8 A. Correct. 9 Q. Okay. And can you turn to Table 1 in 10 Exhibit 11. 11 A. Table 1. Yes. Uh-huh. 12 Q. And in Table 1, do you see glycerol listed 13 there? 14 A. Yes. 15 Q. And this Table 1 is a list of excipients 16 that were tested to prevent aggregation. Is that 17 fair? 18 A. Yes. They were tested for their ability 19 to prevent aggregation. 20 Q. Okay. In the right-hand column, next to 21 glycerol in Table 1 -- 22 A. Uh-huh. 23 Q. -- what do you see there? 24 A. The osmolality required to prevent 25 aggregation. So I think no inhibition of	379 1 CERTIFICATE OF SHORTHAND REPORTER 2 3 I, CRYSTAL HEREFORD, the officer before 4 whom the foregoing deposition was taken, do hereby 5 certify that the foregoing transcript is a true and 6 correct record of the testimony given; that said 7 testimony was taken by me stenographically and 8 thereafter reduced to typewriting under my 9 direction; that reading and signing was not waived; 10 and that I am neither counsel for, related to, nor 11 employed by any of the parties to this case and have 12 no interest, financial or otherwise, in its outcome. 13 IN WITNESS WHEREOF, I have hereunto set my 14 hand and affixed my signature this 23rd day of 15 June 2023. 16 17 18 <i>Crystal Hereford</i> 19 20 21 22 23 24 25
378 1 aggregation was observed with glycerol. 2 Q. Okay. 3 A. Uh-huh. 4 MS. ANTONS: I have no further questions. 5 MR. WEINGARTEN: Okay. We have no further 6 questions as well. 7 We'd like to thank you for your time. 8 Appreciate it. 9 THE WITNESS: Uh-huh. 10 MR. WEINGARTEN: And go enjoy dinner. 11 THE WITNESS: Okay. Thank you. 12 THE VIDEOGRAPHER: This marks the end of 13 the deposition of Dr. John Fraser Wright. We are 14 going off the record at 5:59 p.m. 15 (Proceedings concluded.) 16 17 18 19 20 21 22 23 24 25	

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Exhibit 25



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Transcript of Guang Qu, Ph.D.

Date: June 22, 2023

Case: Genzyme Corporation, et al. -v- Novartis Gene Therapies, Inc., et al.

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Transcript of Guang Qu, Ph.D.

1 (1 to 4)

Conducted on June 22, 2023

1 IN THE UNITED STATES DISTRICT COURT 2 FOR THE DISTRICT OF DELAWARE 3 - - - - - x 4 GENZYME CORPORATION : 5 and AVENTIS INC., : 6 Plaintiffs, : 7 v. : C.A. No. 8 NOVARTIS GENE THERAPIES, INC.; : 21-1736 (RGA) 9 NOVARTIS PHARMACEUTICALS : 10 CORPORATION; and NOVARTIS AG, : 11 Defendants. : 12 - - - - - X 13 CONTAINS HIGHLY CONFIDENTIAL INFORMATION 14 15 Videotaped Deposition of GUANG QU, Ph.D. 16 Conducted Virtually 17 Thursday, June 22, 2023 18 9:41 a.m. EDT 19 20 21 22 23 Job No.: 496642 24 Pages 1 - 238 25 Reported by: Debra A. Whitehead	1 A P P E A R A N C E S 2 ON BEHALF OF PLAINTIFFS AND THE WITNESS: 3 KATHERINE A. HELM, Ph.D., ESQUIRE 4 DECHERT LLP 5 Three Bryant Park 6 1095 Avenue of the Americas 7 New York, New York 10036-6797 8 (212) 698-3500 9 10 ON BEHALF OF DEFENDANTS: 11 M. DAVID WEINGARTEN, Ph.D., ESQUIRE 12 FINNEGAN, HENDERSON, FARABOW, 13 GARRETT & DUNNER, LLP 14 271 17th Street, NW 15 Suite 1400 16 Atlanta, Georgia 30363-6209 17 (404) 653-6457 18 - and - 19 MARTA GARCIA DANESHVA, ESQUIRE 20 FINNEGAN, HENDERSON, FARABOW, 21 GARRETT & DUNNER, LLP 22 Two Seaport Lane 23 Boston, Massachusetts 02210-2001 24 617 646-1635 25
1 Videotaped Deposition of GUANG QU, Ph.D., 2 conducted virtually. 3 4 5 Pursuant to notice, before Debra Ann Whitehead, 6 E-Notary Public in and for the State of Maryland. 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25	1 A P P E A R A N C E S C O N T I N U E D 2 ALSO PRESENT: 3 JACK DUNN, Video Specialist 4 JACKSON SCHUELER, A/V Technician 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

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Transcript of Guang Qu, Ph.D.

2 (5 to 8)

Conducted on June 22, 2023

1	C O N T E N T S	5	1	E X H I B I T S C O N T I N U E D	7
2	EXAMINATION OF GUANG QU, Ph.D.	PAGE	2	QU DEPOSITION EXHIBIT	PAGE
3	By Mr. Weingarten	9	3	Exhibit 14 US Patent and Trademark Office	184
4			4	Records for Patent No. 9,051,542,	
5	E X H I B I T S		5	Bates GENZ_NOV_00000189 - 00000203	
6	(Attached to the Transcript)		6	Exhibit 15 U.S. Patent No. 7,704,721, Bates	186
7	QU DEPOSITION EXHIBIT	PAGE	7	GENZ_NOV_00131278 - 00131289	
8	Exhibit 1 Defendants' Notice of Deposition	17	8	Exhibit 16 Declaration for Utility of Design	188
9	of Guang Qu		9	Application Using an Application	
10	Exhibit 2 3/29/22 Letter from Mr. Rich to	24	10	Data Sheet, Application No.	
11	Dr. Qu, Bates QU0001 - 0003		11	11/141,996, Bates GENZ_NOV_00003914	
12	Exhibit 3 5/25/23 Letter from Ms. Helm to	30	12	Exhibit 17 Provisional Application for	215
13	Dr. Qu, Bates QU0004 - 0007		13	Patent, Application No. 60/639222;	
14	Exhibit 4 Subpoena to Produce Documents,	35	14	Bates GENZ_NOV_00149038 - 00149072	
15	Information, or Objects or to		15	Exhibit 18 Provisional Application for	225
16	Permit Inspection of Premises in		16	Patent, Application No. 60/575997,	
17	a Civil Action		17	Bates NVS-ZOL-00138971 - 00138989	
18	Exhibit 5 Curriculum Vitae, Guang Qu,	51	18		
19	Ph.D., Bates		19		
20	GENZ_NOV_00245873 - 00245877		20		
21	Exhibit 6 Agenda, 6/14/05,	94	21		
22	Bates GENZ_NOV_00245909		22		
23	Exhibit 7 Excerpt from Application No.	120	23		
24	12/661,553, Bates		24		
25	GENZ_NOV_00003911, 00004127		25		
1	E X H I B I T S C O N T I N U E D	6	1	P R O C E E D I N G S	8
2	QU DEPOSITION EXHIBIT	PAGE	2	VIDEO SPECIALIST: Here begins Media	
3	Exhibit 8 Article, "Scaling-up Production	124	3	Number 1 in the videotaped deposition of Guang Qu	
4	of Recombinant AAV Vectors For		4	in the matter of Genzyme Corporation, et al., v	
5	Clinical Applications," by		5	Novartis Gene Therapies, Incorporated, et al.; in	
6	Qu, et al.,		6	the United States District Court for the District	
7	Bates GENZ_NOV_00149008 - 00149014		7	of Delaware; Case Number 21-1736 (RGA).	
8	Exhibit 9 Article, "Recombinant	135	8	Today's date is June 22nd, 2023. The	
9	Adeno-Associated Virus:		9	time on the video monitor is 9:41. The remote	
10	Formulation Challenges and		10	videographer today is Jack Dunn, representing	
11	Strategies for a Gene Therapy		11	Planet Depos. All parties of this deposition are	
12	Vector," by Wright, et al.,		12	attending remotely.	
13	Bates NVS-ZOL-00064429 - 00064433		13	Would counsel please voice-identify	
14	Exhibit 10 U.S. Patent No. 9,408,904	145	14	themselves and state whom they represent.	
15	Exhibit 11 Guang Qu Laboratory Notebook	154	15	MR. WEINGARTEN: Good morning. David	
16	No. 350, Bates		16	Weingarten from Finnegan, Henderson, Farabow,	
17	GENZ_NOV_00011818 - 00012078		17	Garrett & Dunner, on behalf of Defendants	
18	Exhibit 12 Guang Qu Laboratory Notebook	159	18	Novartis, and joined with me is Marta Daneshvar,	
19	No. 351, Bates		19	also from Finnegan.	
20	GENZ_NOV_00012116 - 00012255		20	MS. HELM: Katherine Helm from Dechert,	
21	Exhibit 13 Guang Qu Laboratory Notebook	165	21	representing Plaintiffs Genzyme Corporation and	
22	No. 352, Bates		22	Aventis, as well as the witness.	
23	GENZ_NOV_00012256 - 00012461		23	VIDEO SPECIALIST: The court reporter	
24			24	today is Debbie Whitehead, representing Planet	
25			25	Depos.	

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Transcript of Guang Qu, Ph.D.

3 (9 to 12)

Conducted on June 22, 2023

9 1 The witness will now be sworn. 2 GUANG QU, Ph.D., 3 having been duly sworn, testified as follows: 4 EXAMINATION BY COUNSEL FOR DEFENDANTS 5 BY MR. WEINGARTEN: 6 Q Good morning, Dr. Qu. 7 Can you hear me okay? 8 A Yes, I can hear you well. Thank you. 9 Q Okay. 10 A Good morning. 11 Q Can you please state your name and 12 address, for the record. 13 A Yes. My name is Guang Qu, G-U-A-N-G, Q-U 14 as my last name. I stay in [REDACTED] 15 [REDACTED]. 16 Q And where are you physically located 17 right now for your deposition? 18 A This is the conference room in law firm 19 Dechert -- 20 Q In -- 21 A -- in Philadelphia areas. 22 Q Thank you very much. Appreciate that. 23 That actually gives a segue into some of 24 the ground rules that we'll have during this 25 deposition. And the ground rules will be for both	11 1 for verbal responses. So, you know, yes, no, or 2 whatever the response might be. But try to 3 refrain from a, you know, shaking your head yes or 4 no or sounds that may in the normal conversation 5 may be understood to mean something, but for the 6 purposes of this proceeding only the oral 7 response. Is that okay? 8 A Yes, it is okay. 9 Q Thank you. Now, you know, the day is 10 going to get a little bit long. And, you know, 11 we're cognizant of that. But we're going to do 12 our best to give you breaks throughout the day. 13 I would expect that the breaks will be 14 every hour or so. And so, you know, really what 15 that comes down to is is that if we're not right 16 at the hour and you want a break, just ask for a 17 break. We'll do our best to accommodate you. 18 We may take a break a little bit longer 19 than that, maybe every hour and 15 minutes. We'll 20 see how it goes. In part it depends upon you. It 21 depends on whether you or counsel or the court 22 reporter or we want a break. And those breaks 23 will often be short breaks, and then we'll also, 24 obviously, have a break for lunch. 25 So we'll discuss those when the time
10 1 of our benefits as well as the court reporter's 2 benefit. But first let me ask, have you been 3 deposed before? 4 A No. 5 Q Well, basically the simple rules, and I'm 6 sure that your counsel has provided you some of 7 this guidance, but the rules will be that you're 8 under oath. I'll ask some questions, and, you 9 know, you will be obligated to answer those 10 questions unless you're instructed not to by 11 counsel. 12 When I ask a question, I'm going to 13 assume that you understand my question if you 14 answer the question. So if you have any concerns 15 or need clarification, just ask. You know, I 16 mean, my goal is to make sure my questions are 17 clear, but sometimes they won't be, and I'll 18 expect that you'll ask for clarification. 19 In addition to that, when I'm asking 20 questions, you know, please wait for me to finish 21 asking the question before you start to answer. 22 I'll try to do the same for you. In part that's 23 because the court reporter is not able to sort of 24 document both of us talking at the same time. 25 When I do ask questions, I'm going to ask	12 1 comes. But I want you to be comfortable asking 2 for a break if you need one. The only rule that 3 we have in place for that is that if there is a 4 question pending, then, you know, we ask that you 5 answer the question that's pending. And there 6 might be a short series of questions that I want 7 to get finished before we take that break. But 8 we'll certainly try our best to accommodate. 9 Now, I know that this deposition is being 10 conducted remotely, which means that I'm not 11 sitting in the room there with you. Which would 12 be, you know, I guess practiced back in the olden 13 days. And what I ask is that both counsel have 14 agreed to certain ground rules, and that includes 15 that the witness will be by themselves. 16 And so what I ask you to do is confirm 17 that you are by yourself, nobody else is in the 18 room with you is what I mean by that. And then if 19 somebody does come in the room, absent some 20 technical issue they're trying to solve, that you, 21 you know, let us know so we can pause the 22 deposition, if necessary, and go from there. 23 Do you understand? 24 A Yes, I do. Thank you. 25 Q Yes. I also understand that you have a

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141 1 formulation to use. However, it really depends 2 on, you know, what has been developed. 3 Again, you know, principle-wise, you need 4 the products stabilized, you know, in a stable 5 conditions for certain time period. That's the 6 principle, I would say. So the formulation 7 development, one of the task is, you know, under 8 certain storage condition, the longer, you know, 9 it support the product stability probably will be 10 better formulation. 11 Q And, Doctor, the next sentence in this 12 paragraph says, "Formulation and storage 13 conditions must be amenable to commercial 14 development of a biological product." 15 Is that what it says? 16 A Yes. 17 Q And that's effectively what you're 18 referring to. Right? 19 A That's right. 20 Q And, you know, in order for it to be 21 amenable to commercial development of a biological 22 product, what do you think the minimum storage 23 condition would be? 24 MS. HELM: Objection. 25 A Again, that depends on different --	143 1 of the storage. Basically, this is a -- a 2 product, it can be used for different clinical set 3 and different patient at different state. So you 4 manufacture one lot of the vectors, and then you 5 put them into storage. And then when you -- when, 6 you know, the patient is ready, either the 7 clinical trial-wise or if you commercialize it, it 8 depends on when you are going to deliver the 9 products to the patient. So years, you know, year 10 or years, you know, storage, is not considered, 11 say, for too long. 12 Q I see. Okay. And so if you want to have 13 a formulation that is useful for its intended 14 purpose, for example if it's given to a patient in 15 AAV, you're talking about something that can be 16 stored for a year, approximately? 17 A Yeah. 18 Q And if you look on this page -- again 19 this is Exhibit 9 -- we're going to focus on Page 20 Bates Number 430. That's the page you're on. If 21 you go towards the bottom of that page, there's a 22 paragraph that begins, "While the development of." 23 Do you see that? 24 A Okay, I do see it. 25 Q Okay. And it's talking about the
142 1 depends on what products, you know, people are 2 talking -- talking about. 3 Some products, you know, it just, you 4 know, has to be used in a short time period. It's 5 not going to be, you know, stabilized for, you 6 know, long durations. 7 Let's focus on the AAV as a products. I 8 mean, I can give you some examples, like, you 9 know, shelf life is just, you know, couple of 10 weeks, you know, in terms of short storage 11 conditions. 12 Q Okay. That's -- 13 A Other than -- I'm sorry. 14 Q No. Go ahead. Finish your answer. 15 A Nowadays for the cell therapy part, you 16 know, gene therapy, cell therapy, you know, the 17 cell therapy sometimes it just -- you know, you 18 take the cells from patient. And then you do your 19 manufacturings. Right after you finish the 20 characterization, you deliver it back to the 21 patient. So this has to be, you know, individuals 22 products to measure, you know, how long is the 23 storage durations. 24 So for AAV products, nowadays people are 25 talking about, you know, year, how years in term	144 1 development of buffer systems, and you want to 2 minimize loss of vector infectious titer. 3 Do you see that? That's the first 4 sentence? 5 A Yes, I do. 6 Q And then the next sentence after that 7 says, "For such nonfrozen formulations, a 8 reasonable target for AAV vector stability for 9 commercial applications is minimal loss, not less 10 than 10 percent, of infectious activity during a 11 period of greater than or equal to two years." 12 Is that right? 13 A Yes, you read it right. Yes. 14 Q Okay. All right. Let's go to Bates 15 number ending in 431, which is the next page. 16 Well, you know what? Let's put this 17 exhibit aside. 18 Doctor, you've talked about -- we've 19 heard the words "adenovirus," we've heard the 20 words "parvovirus," we've heard the words "AAV" or 21 abbreviated "AAV." What is lentivirus? 22 A Lentivirus is another group of virus. 23 Again, you know, if we talk about AAV belong to 24 parvovirus, adenovirus is another group, class of 25 virus. And then the lentivirus is, you know,

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Transcript of Guang Qu, Ph.D.

60 (237 to 240)

Conducted on June 22, 2023

237 1 We are going off the record at 17:28. 2 (A recess was taken.) 3 VIDEO SPECIALIST: We are going back on 4 the record. The time is 17:39. 5 MR. WEINGARTEN: Dr. Qu, subject to your 6 attorney having any questions, we have no more 7 questions. 8 MS. HELM: Dr. Qu, I have no questions 9 for you. 10 THE WITNESS: Thank you. 11 MR. WEINGARTEN: All right. Dr. Qu, 12 thank you very much for your time today. I really 13 appreciate it. We thank you for your time, and 14 have a great day. 15 VIDEO SPECIALIST: Stand by. 16 This marks the end of the deposition of 17 Guang Qu. We are going off the record at 17:39. 18 (Off the record at 5:39 p.m. EDT) 19 20 21 22 23 24 25	
238 1 CERTIFICATE OF SHORTHAND REPORTER - NOTARY PUBLIC 2 I, Debra A. Whitehead, the officer before whom 3 the foregoing proceedings were taken, do hereby 4 certify that the foregoing transcript is a true 5 and correct record of the proceedings; that said 6 proceedings were taken by me stenographically and 7 thereafter reduced to typewriting under my 8 supervision; that reading and signing was not 9 discussed; and that I am neither counsel for, 10 related to, nor employed by any of the parties to 11 this case and have no interest, financial or 12 otherwise, in its outcome. 13 IN WITNESS WHEREOF, I have hereunto set my hand 14 and affixed my notarial seal this 24th day of 15 June, 2023. 16 17 My commission expires: 18 April 30, 2027 19 20 21  22 ----- 23 E-NOTARY PUBLIC IN AND FOR THE 24 STATE OF MARYLAND 25	

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