

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

GENZYME CORPORATION and	)	
AVENTIS INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	
	)	C.A. No. _____
NOVARTIS GENE THERAPIES, INC. and	)	
NOVARTIS PHARMACEUTICALS	)	JURY TRIAL DEMANDED
CORPORATION	)	
	)	
Defendants.	)	
	)	

COMPLAINT

This is a claim for willful patent infringement arising out of abuse of the discovery process in the related action, *Genzyme Corporation et al. v. Novartis Gene Therapies, Inc.*, et al, C.A. No. 1:21-cv-01736-RGA (“*Genzyme I*”). During *Genzyme I*, plaintiffs Genzyme Corporation (“Genzyme Corp.”) and Aventis Inc. (“Aventis”) (collectively, “Genzyme”) made a routine request for access to the Biologics License Application (“BLA”) for Zolgensma[®], but rather than produce the information, Defendants Novartis Gene Therapies, Inc. and Novartis Pharmaceuticals Corporation (“Novartis”) refused to produce the critical portions of the BLA and hid material information from discovery. When Novartis finally produced the BLA under a Court Order, it became clear that the BLA contained unequivocal evidence establishing infringement of Plaintiffs’ U.S. Patent No. 10,429,288 (the “’288 Patent”). By then, it was too late to add the ’288 Patent infringement claim to *Genzyme I*.

Plaintiffs now file this separate action, as directed by this Court, to seek redress for patent infringement. Plaintiffs seek an expedited schedule and a finding of willfulness under, among other things, factors 3 and 9 of the *Read* factors, which make “the infringer’s behavior as a party

to the litigation” and “whether the infringer attempted to conceal its misconduct” key factors in the willfulness analysis. *Read Corp. v. Portec, Inc.*, 970 F.2d 816, 827 (Fed. Cir. 1992).

PARTIES

1. Plaintiff Genzyme is a corporation organized and existing under the laws of the Commonwealth of Massachusetts, having its principal place of business at 450 Water Street, Cambridge, Massachusetts 02141.

2. Plaintiff Aventis is a limited liability company organized and existing under the laws of the State of Delaware, having its principal place of business at 55 Corporate Drive, Bridgewater, New Jersey 08807. Genzyme is a wholly-owned subsidiary of Aventis.

3. On information and belief, Novartis Gene Therapies, Inc. is a corporation organized and existing under the laws of Delaware, having its corporate offices and principal place of business at 2275 Half Day Road, Suite 203, Bannockburn, Illinois 60015. On information and belief, Novartis Gene Therapies has a registered agent for service of process, Corporation Service Company, 251 Little Falls Drive, Wilmington, Delaware 19808.

4. On information and belief, Novartis Pharmaceuticals Corporation is a corporation organized and existing under the laws of Delaware, having its corporate offices and principal place of business at 1 Health Plaza, East Hanover, New Jersey 07936. On information and belief, Novartis Pharmaceuticals Corporation has a registered agent for service of process, Corporation Service Company, 251 Little Falls Drive, Wilmington, Delaware 19808. On information and belief, Novartis Pharmaceuticals Corporation is the direct or indirect parent of Novartis Gene Therapies, Inc. and has at all times directed and controlled the infringing actions of its subsidiary.

NATURE OF ACTION

5. This is an action for infringement of United States Patent No. 10,429,288 (the “288 Patent”). This action is based upon the Patent Laws of the United States, 35 U.S.C. § 100, *et seq.*

JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over this action under 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over Novartis Gene Therapies, Inc. because Novartis Gene Therapies, Inc. is incorporated in Delaware, knowingly transacts business in Delaware, maintains a registered agent in Delaware, and, on information and belief, has engaged in, and made meaningful preparations to engage in, infringing conduct in Delaware.

8. This Court has personal jurisdiction over Novartis Pharmaceuticals Corporation because Novartis Pharmaceuticals Corporation is incorporated in Delaware, knowingly transacts business in Delaware, maintains a registered agent in Delaware, avails itself of this Court in numerous lawsuits that it and/or its related entities have filed before this Court, and, on information and belief, has engaged in, and made meaningful preparations to engage in, infringing conduct in Delaware.

9. Venue is proper in this district pursuant to 28 U.S.C. § 1400(b) with respect to Novartis Gene Therapies, Inc. for at least the reason that it resides in this district.

10. Venue is proper in this district pursuant to 28 U.S.C. § 1400(b) with respect to Novartis Pharmaceuticals Corporation for at least the reason that it resides in this district.

FACTUAL BACKGROUND

The '288 Patent

11. It has long been recognized that certain diseases are caused by missing or defective genes, resulting in the inability of the body to produce key proteins. The result can be devastating, but the options for treating such genetic diseases have been limited. The radical approach taken by gene therapy is to attack the problem at the source—the patient's own genome—by replacing the defective or missing gene with a full working copy, referred to as a transgene. Gene therapy is at the cutting edge of medical technology, and the problems faced both in the delivery of transgenes and their manufacture are daunting.

12. Gene therapy can be performed by taking advantage of one of the body's age-old enemies, viruses, which have evolved to enter human cells. By removing part of the native viral DNA and substituting the DNA of the desired human transgene, a recombinant virus can be created that can enter cells and then deliver a desired human gene into a cell. At the time of the invention of the '288 Patent, it was known that in the right circumstances a modified adeno-associated virus ("AAV") could be used to achieve the delivery of the transgene. These genetically-engineered versions of the adeno-associated virus are known as recombinant adeno-associated virus vectors ("rAAV").

13. The process of creating an rAAV-based therapeutic involves the initial creation of the vector genome or genetic payload carrying the transgene, followed by encapsulation of the vector genome in a protein shell called a capsid. Packaging the vector genome in the capsid is not a perfect process resulting in a mixture of (1) properly encapsulated vector genome, (2) empty capsids that contain no vector genome, and (3) partially filled capsids that contain a fragmented or incomplete vector genome. Empty capsids and partially filled capsids are highly undesirable, and characterizing and purifying the preparations is a major difficulty in commercial

manufacturing of rAAV therapies. In particular, it is critical to avoid introducing unwanted gene fragments and other impurities into patients. The Food and Drug Administration (“FDA”) has identified these issues as raising important health concerns and has focused heavily on the manufacturing process in evaluating which therapies will obtain marketing approval. *See, e.g.*, Cellular, Tissue, and Gene Therapies Advisory Committee, “Toxicity Risks of Adeno-associated Virus (AAV) Vectors for Gene Therapy,” FOOD AND DRUG ADMINISTRATION, Sept. 2-3, 2021, at §§ 2.3-2.4.1, 2.4.3, <https://www.fda.gov/media/151599/download>.

14. Purifying the properly formed capsids is an important and necessary step in the manufacturing process. Prior to the invention claimed in the ’288 Patent, determining the quality of the DNA content of recombinant viral DNA vectors and viral capsids required separate analytical methods, such as immunoassays or Southern blot analysis. These techniques required antibodies that bind to a specific capsid protein or a sequence-specific nucleotide probe. But before the invention described in the ’288 Patent, there was not a single assay that could distinguish between the properly-formed capsids and the undesired species—empty capsids and partially-filled capsids—on a quantitative basis.

15. The invention described in the ’288 Patent is directed towards solving that problem. Catherine R. O’Riordan and Brenda Burnham, the inventors of the subject matter claimed in the ’288 Patent, developed an assay using analytical ultracentrifugation (“AUC”)—a means of evaluating the molecular weight and the hydrodynamic and thermodynamic properties of a protein or other macromolecule. The AUC techniques described and claimed in the ’288 Patent allow for the detection of rAAV species, including full capsid particles, empty viral capsids with no rAAV genomes, and rAAV partially filled variants, regardless of the nucleotide sequence of the recombinant viral genome or the serotype of the recombinant viral capsid. In doing so, the

claimed AUC methods can be used to assess, quantitatively and qualitatively, drug product for homogeneity, purity, and consistency. Thus, the '288 Patent represents a significant advancement to ensure consistency in the final drug and/or gene therapy product.

16. On October 1, 2019, the United States Patent & Trademark Office ("USPTO") duly and legally issued the '288 Patent, titled "Analytical Ultracentrifugation for Characterization of Recombinant Viral Particle." The '288 Patent is assigned to Genzyme Corp. A true and correct copy of the '288 Patent is attached as Exhibit A.

17. The '288 Patent issued from U.S. Application No. 15/544,498, filed on July 18, 2017, which is a National Stage Entry of PCT/US2016/013947, which claims priority to U.S. Provisional Patent Application No. 62/105,714 filed on January 20, 2015.

18. The '288 Patent expires on January 19, 2036. It has been valid and enforceable at all times since it issued and remains valid and enforceable.

19. The claims of the '288 Patent are generally directed to methods to characterize a preparation of recombinant adeno-associated viral particles using analytical ultracentrifugation.

By way of example, claim 1 of the '288 Patent states:

A method of characterizing a preparation of recombinant adeno-associated viral (AAV) particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value ($C(s)$) versus the sedimentation coefficient in Svedberg units (S), and
- c) integrating the area under each peak in the $C(s)$ distribution to determine the relative concentration of each peak, wherein each peak represents a species of recombinant AAV particle.

Zolgensma®

20. On April 9, 2018, Novartis AG announced that it had entered into an agreement to acquire AveXis, Inc. On May 15, 2018, the transaction closed, and AveXis, Inc. became a wholly-owned indirect subsidiary of Novartis AG.

21. On May 24, 2019, AveXis, Inc. obtained FDA approval to market Zolgensma® (onasemnogene abeparvovec-xioi) as a gene therapy product intended to treat certain children less than two years of age with Spinal Muscular Atrophy, known as SMA. Zolgensma® is an adeno-associated virus-based gene therapy product that delivers a copy of the human survival motor neuron (SMN) gene into target motor neuron cells of the child, which results in expression of the SMN protein in the motor neuron cells, thus treating SMA. Following FDA approval, AveXis, Inc. (now known as Novartis Gene Therapies, Inc.) promptly began sales and active promotion of the product in the United States for the treatment of SMA. A true and correct copy of the current Zolgensma® package insert dated October 2021 is attached as Exhibit B.

22. In manufacturing Zolgensma® drug product, upon information and belief, Defendants determine the relative amount of the empty and full particles in their rAAV preparations utilizing the claimed analytical ultracentrifugation techniques of the '288 Patent.

23. On information and belief, Zolgensma® has been and is currently manufactured by Novartis Gene Therapies, Inc. in Libertyville, Illinois and Durham, North Carolina. On information and belief, Zolgensma® was previously also manufactured in Longmont, Colorado.

The *Genzyme I* Litigation

24. On February 23, 2022, Plaintiffs filed a First Amended Complaint against Defendants in *Genzyme Corp. et al. v. Novartis Gene Therapies, Inc. et al.*, C.A. No. 21-cv-01736 (D. Del.) (the "*Genzyme I* action"). The complaint alleged that Defendants infringe United States Patent

Nos. 6,596,535; 7,125,717; 7,785,888; 7,846,729; 8,093,054; and 9,051,542 through the unauthorized manufacture, use, and sale of rAAV vectors for their gene therapy drug Zolgensma®.

25. In connection with the *Genzyme I* action, Plaintiffs requested a copy of the BLA filed with the FDA. Rather than produce these materials, as routinely happens in pharmaceutical litigation, Defendants stalled and then refused to produce the complete sections of the BLA pertaining to the manufacture and testing of Zolgensma®. Defendants' behavior was suspicious, and Plaintiffs consistently pressed for the discovery.

26. Specifically, Plaintiffs served Paragraph 4(a) disclosures on Defendants on April 18, 2022. One month later, Defendants produced Paragraph 4(b) initial disclosures, including only heavily redacted pages from the BLA that were out of the order in which they were provided to the FDA. The next day, Plaintiffs highlighted deficiencies in Defendants' production and requested a conference to rectify the deficiencies. Defendants took the position that its obligations were satisfied by producing "relevant document from modules 2 and 3 of the BLA". A few days later, on May 27, 2022 and despite their prior representations, Defendants produced additional fragments of the BLA, but still out of order and with heavy redactions.

27. Plaintiffs continued to press on these deficiencies in written and oral communications between counsel throughout the summer months. Defendants, however, continued to withhold key sections of the BLA and disagreed with Plaintiffs that the issue was ripe for court intervention. In September 2022, following no response from Defendants, Plaintiffs informed Defendants they were at an impasse and enumerated several documents comprising the BLA that generally contained inappropriate redactions. Defendants repeatedly disagreed there was any impasse and

requested further meet-and-confer discussions, while actively avoiding such discussions and refusing to produce the requested BLA documents.

28. Finally, on November 29, 2022, after Defendants again refused to produce the unredacted portions of the Zolgensma® BLA, the parties initiated the Court's procedure for resolving discovery disputes and Plaintiffs submitted their letter related to Defendants' redactions (D.I. 89). On December 6, 2022, this Court granted Plaintiffs' motion, ordering Defendants to produce unredacted versions of the relevant sections of the BLA by December 13, 2022 (D.I. 93). On December 12, 2022, Defendants made a production, but inaccurately represented that the production was in the same order and format as it was produced to the FDA. The production is accompanied by a 21-page, single-spaced appendix showing the many ways in which the previous productions were not made in the order in which the BLA was submitted in the normal course to the FDA. Plaintiffs promptly requested the reordering of BLA documents and held a meet-and-confer regarding discrepancies in the Bates numbers of the BLA page numbering as produced.

29. It was not until January 20, 2023, that Defendants acknowledged that the previously-produced BLA was produced out of order relative to its arrangement in the ordinary course of business and not in the order in which it was submitted to the FDA. The Defendants then finally produced the BLA in the proper order as kept in the normal course of business.

30. Due to Defendants' delay and obstruction in connection with producing the BLA, Plaintiffs were unable to move for leave to file a second amended complaint adding the '288 Patent in the *Genzyme I* action until February 8, 2023. As a direct result of Defendants' delay, this Court determined that it was "too late" to add the '288 Patent into the *Genzyme I* action and that Plaintiffs should instead bring a new suit on the '288 Patent.

31. The delay in providing the BLA has caused material prejudice to Plaintiffs, as the trial of the '288 Patent will not take place in March 2024 concurrently with the scheduled trial in the *Genzyme I*.

COUNT I
INFRINGEMENT OF THE '288 PATENT

32. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 31 above as though fully set forth herein.

33. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma[®] infringes one or more claims of the '288 Patent, including but not limited to claims 1, 2, 4, 5, 6, 7, 8, and 12, under 35 U.S.C. §§ 271(a) and/or (b).

34. The '288 Patent has eight independent claims, claim 1, claim 2, claim 4, claim 5, claim 6, claim 7, claim 8, and claim 12. Claim 1 recites:

A method of characterizing a preparation of recombinant adeno-associated viral (AAV) particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S), and
- c) integrating the area under each peak in the C(s) distribution to determine the relative concentration of each peak, wherein each peak represents a species of recombinant AAV particle.

35. On information and belief, Zolgensma[®] is a preparation of recombinant adeno-associated (AAV) particles in which a method is used to characterize the preparation of recombinant AAV particles. More specifically it is believed that the method of characterization is achieved by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is

monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, and integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particle. Thus, Zolgensma[®] infringes at least independent claim 1 of the ’288 Patent.

36. Claim 2 recites:

A method to assess vector genome integrity of recombinant AAV particles in a preparation of recombinant AAV particles comprising

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value C(s) versus the sedimentation coefficient in Svedberg units (S), and
- c) identifying species of recombinant AAV particles in the preparation by presence of peaks on the plot corresponding to an S value, wherein the genome size of a particular species of recombinant AAV particles is calculated by comparing the S value of the species to a standard curve generated by S values of recombinant AAV particles comprising encapsidated AAV genomes of known nucleotide sizes.

37. On information and belief, Zolgensma[®] is also a composition of recombinant AAV particles in which vector genome integrity is assessed in the preparation of recombinant AAV particles. On information and belief, a method is used to assess vector genome integrity by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, and identifying the species of recombinant AAV particles by presence of peaks on the plot corresponding to an S value. Thus, Zolgensma[®] infringes at least independent claim 2 of the ’288 Patent.

38. Claim 4 recites:

A method to determine the presence of empty capsids or capsid particles comprising variant sized recombinant AAV genomes in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, and
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S), wherein the presence of one or more peaks other than the peak for full capsid particles comprising intact recombinant AAV genomes indicates that presence of capsid particles comprising variant sized genomes and/or empty capsids.

39. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the presence of empty capsids or capsid particles comprising variant sized recombinant AAV genomes is determined in the preparation of recombinant AAV particles. On information and belief, a method is used to determine the presence of empty capsids or capsid particles comprising variant sized recombinant AAV genomes by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, and identifying the presence of capsid particles comprising variant sized genomes and/or empty capsids through the presence of one or more peaks other than the peak for full capsid particles. Thus, Zolgensma[®] infringes at least independent claim 4 of the ’288 Patent.

40. Claim 5 recites:

A method of measuring the relative amount empty capsids in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,

- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S),
- c) integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles, and
- d) comparing the amount of recombinant AAV particles having an S value corresponding to empty capsid particles to the amount of recombinant AAV particles having an S value corresponding to recombinant AAV particles comprising intact AAV genomes or the total amount of recombinant AAV particles in the preparation.

41. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the relative amount of empty capsids is measured in the preparation of recombinant AAV particles. On information and belief, a method is used to measure the relative amount of empty capsids in a preparation of recombinant AAV particles by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value ("C(s)") versus the sedimentation coefficient in Svedberg units, integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles, and comparing the amount of recombinant AAV particles with an S value for an empty capsid particle to those with an S value corresponding to recombinant AAV particles with intact AAV genomes or the total amount of recombinant AAV particles in the preparation. Thus, Zolgensma[®] infringes at least independent claim 5 of the '288 Patent.

42. Claim 6 recites:

A method of measuring the relative amount of capsid particles comprising variant recombinant AAV genomes or empty AAV capsid particles in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S),
- c) integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles,
- d) comparing the amount of recombinant AAV particles having an S values that do not correspond to recombinant AAV particles comprising intact AAV genomes to the amount of recombinant AAV particles having an S value that corresponds to recombinant AAV particles comprising intact AAV genomes or to the total amount of recombinant AAV particles in the preparation.

43. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the relative amount of capsid particles comprising variant recombinant AAV genomes or empty AAV capsid particles is measured in the preparation of recombinant AAV particles. On information and belief, a method is used to measure the relative amount of capsid particles comprising variant recombinant AAV genomes or empty AAV capsid particles by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles, and comparing the amount of recombinant AAV particles with an S value that do not correspond to recombinant AAV particles comprising intact AAV genomes to the amount of recombinant AAV particles having an S value that corresponds to recombinant AAV particles comprising intact AAV genomes or to the total amount of recombinant AAV particles in the preparation. Thus, Zolgensma[®] infringes at least independent claim 6 of the ’288 Patent.

44. Claim 7 recites:

A method of measuring the relative amount of capsid particles comprising variant recombinant AAV genomes in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S),
- c) integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles,
- d) comparing the amount of recombinant AAV particles having an S values that do not correspond to recombinant AAV particles comprising intact AAV genomes or empty capsid particles to the total amount of recombinant AAV particles in the preparation.

45. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the relative amount of capsid particles comprising variant recombinant AAV genomes is measured in the preparation of recombinant AAV particles. On information and belief, a method is used to measure the relative amount of capsid particles comprising variant recombinant AAV genomes by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles, and comparing the amount of recombinant AAV particles with an S value that does not correspond to recombinant AAV particles comprising intact AAV genomes or empty capsid particles to the total amount of recombinant AAV particles in the preparation. Thus, Zolgensma[®] infringes at least independent claim 7 of the ’288 Patent.

46. Claim 8 recites:

A method of measuring the relative amount of recombinant AAV particles comprising intact AAV genomes in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S),
- c) integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles,
- d) comparing the amount of recombinant AAV particles having an S values corresponding to recombinant AAV particles comprising intact AAV genomes to the amount of recombinant AAV particles having an S value corresponding to empty capsid particles, to capsid particles comprising variant recombinant AAV genomes, and/or to the total amount of recombinant AAV particles in the preparation.

47. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the relative amount of recombinant AAV particles comprising intact AAV genomes is measured in the preparation of recombinant AAV particles. On information and belief, a method is used to measure the relative amount of recombinant AAV particles comprising intact AAV genomes by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, plotting the differential sedimentation coefficient distribution value (“C(s)”) versus the sedimentation coefficient in Svedberg units, integrating the area under each peak in the C(s) distribution to determine the relative concentration of each species of recombinant AAV particles, and comparing the amount of recombinant AAV particles with an S value that corresponds to recombinant AAV particles comprising intact AAV genomes to the amount of recombinant AAV particles having an S value corresponding to empty capsid particles,

to capsid particles comprising variant recombinant AAV genomes, and/or to the total amount of recombinant AAV particles in the preparation. Thus, Zolgensma[®] infringes at least independent claim 8 of the '288 Patent.

48. Claim 12 recites:

A method of determining the heterogeneity of recombinant AAV particles in a preparation of recombinant AAV particles comprising the steps of

- a) subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals,
- b) plotting the differential sedimentation coefficient distribution value (C(s)) versus the sedimentation coefficient in Svedberg units (S), wherein the presence of peaks in addition to the peak representing capsids comprising an intact AAV genome indicates heterogeneity of recombinant particles in the preparation.

49. On information and belief, Zolgensma[®] is a preparation of recombinant AAV particles in which the heterogeneity of recombinant AAV particles is measured in the preparation of recombinant AAV particles. On information and belief, a method is used to measure heterogeneity of recombinant AAV particles by subjecting the preparation to analytical ultracentrifugation under boundary sedimentation velocity conditions wherein the sedimentation of recombinant AAV particles is monitored at time intervals, and plotting the differential sedimentation coefficient distribution value ("C(s)") versus the sedimentation coefficient in Svedberg units, and identifying the presence of peaks in addition to the peak representing capsids comprising an intact AAV genome. Thus, Zolgensma[®] infringes at least independent claim 12 of the '288 Patent.

50. Plaintiffs have suffered damages as a result of Defendants' infringement of the '288 Patent.

51. Defendants had knowledge of the '288 Patent at least as early as February 8, 2023, when Plaintiffs sought to amend the complaint in the *Genzyme I* action to assert the '288 Patent against Defendants.

52. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '288 Patent, Defendants knew or should know that their actions infringe the '288 Patent. Defendants sought to conceal that infringement from Plaintiffs by engaging in an unreasonable and extended refusal to produce unredacted portions of the BLA for Zolgensma® that would show their infringement. Through redactions, reordering of documents, and refusal to produce portions of documents that were clearly relevant to the litigation in the *Genzyme I* action and responsive to requests for production in that litigation, Defendants engaged in an intentional effort to hide their infringement of the '288 Patent. *See supra* ¶¶ 24-31. Indeed, Defendants only provided this critical information in its proper form, because the Court ordered them to do so.

53. Even after the Court ordered the production of the BLA and required Genzyme to file a new action, Defendants continued in obstructionist behavior, refusing to agree that materials in the first action could be reproduced in the new case. Such conduct constitutes evidence of willfulness under at least *Read* factor 3, "the infringer's behavior as a party to the litigation" and factor 9, "whether the infringer attempted to conceal its misconduct." As explained above, *see supra* ¶¶ 24-31, Defendants engaged in obstructionist conduct over the course of ten months in order to withhold information from Plaintiffs regarding Zolgensma®'s infringement of the '288 Patent, ultimately succeeding in preventing Plaintiffs from adding the '288 Patent into the *Genzyme I* action. Defendants are also corporations that are of significant size with substantial revenue. Additionally, upon information and belief, Defendants' obstructionist conduct was intentionally done in order to conceal their infringement of the '288

Patent from Plaintiffs such that *Read* factors (8) and (9) further support an award of enhanced damages. *Read Corp. v. Portec, Inc.*, 970 F.2d 816, 827-828 (Fed. Cir. 1992). To the extent that Defendants continue their dilatory tactics in this new action, it would only serve as further evidence of willfulness.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court:

- A. Enter judgment that Defendants have infringed the '288 Patent.
- B. Enter judgment that Defendants' infringement of the '288 Patent is willful;
- C. Award damages adequate to compensate Plaintiffs for Defendants' infringement, including increased damages up to three times the amount found or assessed, together with pre-judgment and post-judgment interest and costs, under 35 U.S.C. §§ 284;
- D. Award treble damages under 35 U.S.C. § 284 for each day that the trial in this action is delayed beyond March 25, 2024, the date on which the original trial in this action would have taken place but for the Defendants' discovery misconduct;
- E. Enter judgment that this case is exceptional and award Plaintiffs their reasonable attorneys' fees, costs, and expenses, under 35 U.S.C. § 285; and
- F. Award such other and further relief as this Court may deem just and proper.

DEMAND FOR JURY TRIAL

Plaintiffs hereby demand a trial by jury as to all issues so triable.

WILKS LAW, LLC

/s/ David E. Wilks

David E. Wilks (Del. Bar # 2793)

Scott B. Czerwonka (Del. Bar # 4844)

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