IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENZYME CORPORATION and AVENTIS INC.,	)	
Plaintiffs,	)	
v.	)	
	)	C.A. No. 21-1736 (RGA)
NOVARTIS GENE THERAPIES, INC., NOVARTIS PHARMACEUTICALS CORPORATION, and NOVARTIS AG	)	JURY TRIAL DEMANDED
Defendants.	)	

FIRST AMENDED COMPLAINT

Plaintiffs Genzyme Corporation ("Genzyme") and Aventis Inc. ("Aventis") (collectively, "Plaintiffs"), for their Complaint against Defendants Novartis Gene Therapies, Inc., Novartis Pharmaceutical Corporation, and Novartis AG (collectively, "Novartis" or "Defendants"), allege as follows:

Nature of the Action

1. This is a civil action under the Patent Act, 35 U.S.C. § 1 *et seq.*, for infringement of United States patents. Specifically, Plaintiffs allege that Defendants infringe United States Patent No. 6,596,535 (the "'535 Patent"); United States Patent No. 7,125,717 (the "'717 Patent"); United States Patent No. 7,785,888 (the "'888 Patent"), United States Patent No. 7,846,729 (the "'729 Patent"), United States Patent No. 8,093,054 (the "'054 Patent"), and United States Patent No. 9,051,542 (the "'542 Patent") (collectively, the "Asserted Patents") through the unauthorized manufacture, use, and sale of recombinant adeno-associated virus vectors ("rAAV vectors") for their gene therapy drug Zolgensma®.

The Parties

2. Plaintiff Genzyme is a corporation organized and existing under the laws of the Commonwealth of Massachusetts, having its principal place of business at 50 Binney Street, Cambridge, Massachusetts 02142.

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

4. 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 may be served via its registered agent, Corporation Service Company, 251 Little Falls Drive, Wilmington, Delaware 19808.

5. 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 may be served via its registered agent 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.

6. On information and belief, Novartis AG is a corporation organized and existing under the laws of Switzerland, having its corporate offices and principal place of business at Fabrikstrasse 2, 4056 Basel, Switzerland. On information and belief, Novartis AG is the direct

or indirect parent of Novartis Pharmaceuticals Corporation and Novartis Gene Therapies, Inc. and has at all times directed and controlled the infringing actions of its subsidiaries.

Jurisdiction and Venue

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

8. This Court has personal jurisdiction over Novartis Gene Therapies, Inc. for at least the reasons that 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.

9. 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.

10. On information and belief, this Court may exercise personal jurisdiction over Novartis AG because of its contacts with this forum, including its regularly and intentionally doing business here, availing itself of this Court in numerous lawsuits that it and/or its related entities have filed before this Court, and/or committing acts giving rise to this lawsuit here. Alternatively, on information and belief, this Court may exercise personal jurisdiction over Novartis AG under Federal Rule of Civil Procedure 4(k)(2).

11. 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.

12. 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.

13. Venue is proper in this district pursuant to at least 28 U.S.C. § 1391(b) and (c) with respect to Novartis AG.

Statement of Facts

Background of the Technology at Issue

14. The Asserted Patents relate to recombinant viral vectors useful in gene therapy (among other things), as well as methods for the preparation, use, and/or storage of such vectors. Gene therapy is a groundbreaking medical technique to treat or cure disease by modifying a person's own genes. One mechanism by which gene therapy can work is by introducing functional copies of a gene (called a "transgene") into a patient's cells that have a faulty or missing natural version of the gene. By doing so, gene therapy can treat, or even cure, a genetic disorder.

15. Gene therapy can be performed by packaging and delivering a transgene to the cells of a patient using recombinant viral vectors, such as recombinant adeno-associated virus (rAAV) vectors that are incorporated into adeno-associated virus (AAV). However, obtaining sufficient levels of transgene expression can be a hurdle for effective gene therapy. In some cells, expression of the transgene necessary to provide a therapeutic effect can be slow to initiate or does not initiate at all.

16. When an AAV virus containing a rAAV vector is administered to a patient, a single-stranded viral vector DNA containing the transgene is transferred into a target cell. The

incoming single-stranded DNA must then be converted to a double-stranded DNA molecule by the target cell's own cellular mechanisms. This formation of double-stranded DNA is a key rate-limiting step in the transfer of genetic material from the rAAV vector and the ultimate ability for expression of the transgene in a cell. Thus, double-stranded DNA formation is needed for efficient expression of a therapeutic protein and for functional gene therapy.

17. The inventor of the '535, '717, '888, '729, and '054 Patents (collectively the "Carter Patents"), Dr. Barrie J. Carter, discovered that rAAV vector DNA can be engineered to self-adopt a double-stranded conformation upon delivery to a target cell, and can be packaged in a manner to facilitate this conformation so that the cellular processes needed to express the therapeutic protein encoded by the vector transgene can begin immediately once the vector is introduced into the cell. In other words, the vectors described in the Carter Patents eliminate the need for the target cell to convert single-stranded DNA to double-stranded DNA. The Carter Patents refer to this technology as vectors with "intrastrand base pairing," which are also widely known in the field as "self-complementary vectors." Using the intrastrand base pairing technology of the Carter Patents, the onset of gene expression is increased, so more cells can receive genetic material at a given dose of rAAV vector or the rAAV vector can be effective at a lower dose as compared to any prior rAAV vectors. This discovery formed the basis for later improvements on different ways to generate self-complementary vectors, which have now been incorporated into important gene therapy platforms.

18. Another challenge in effectively implementing gene therapy is ensuring that it can be delivered in a safe, efficient way. A complication in delivery is the low stability and solubility of rAAV vector particles in buffered solutions, which may lead to aggregation of rAAV vector particles (particularly at higher concentrations of rAAV). Aggregation can negatively impact

virus biodistribution and transduction efficiency, and can also increase immunogenicity following virus administration. The inventors of the '542 Patent, John Fraser Wright and Guang Qu, solved these problems in discovering that certain high ionic strength solutions for preparing and storing rAAV viruses can prevent significant aggregation of virus particles at the viral concentrations needed for effective gene therapy.

19. Thus, the Asserted Patents represent significant advances that allow for functional gene therapy.

The Carter Patents were Licensed

20. Building upon the technology of the Asserted Patents, Dr. Richard Samulski's laboratory at the University of North Carolina identified one way to form the intrastrand base pairing vectors described by the Asserted Patents. In May 2013, Asklépios BioPharmaceutical, Inc ("AskBio"), which was co-founded by Dr. Samulski, entered into a license agreement with Genzyme, whereby AskBio received certain rights to the Carter Patents. The rights that Genzyme licensed to AskBio included a limited right to sublicense. Notably, the rights Genzyme licensed to AskBio expressly excluded the field of treating spinal muscular atrophy (SMA). AskBio therefore could not have sublicensed rights related to treating SMA.

21. Two years later, on May29, 2015, upon information and belief, AskBio entered into a licensing agreement with AveXis, Inc. (now Novartis Gene Therapies, Inc.), which granted AveXis, Inc. certain rights to AskBio's "self-complementary" patent portfolio. On information and belief, based on, at least the due diligence related to the AskBio-AveXis, Inc. license, Novartis Gene Therapies, Inc. was aware of the Carter Patents before it began marketing Zolgensma®. Because AskBio had no rights to the Carter Patents in relation to SMA, however, its license to AveXis, Inc. could not include any rights related to the treatment of SMA.

22. Despite the express carve-out of SMA from the Genzyme-AskBio license (and therefore the AskBio-AveXis, Inc. license), on information and belief AveXis, Inc. used the technology licensed from AskBio to generate Zolgensma® for treatment of SMA.

Zolgensma®

23. 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. The closing of the transaction was accompanied by a press release quoting the CEOs of Novartis AG and Novartis Pharmaceuticals Corporation regarding the relationship with AveXis, Inc.

24. 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 SMA. On September 2, 2020, Novartis AG announced that AveXis, Inc. had been renamed and rebranded as Novartis Gene Therapies, Inc.

25. Following FDA approval of Zolgensma®, AveXis, Inc. promptly began sales and active promotion of the product in the United States for the treatment of SMA, and has continued sales and promotion after being renamed Novartis Gene Therapies, Inc. Zolgensma® is a gene therapy product indicated for use in certain children less than two years old with SMA. A true and correct copy of the current Zolgensma® package insert dated October 2021 is attached as Exhibit A.

26. Zolgensma® is an adeno-associated virus (AAV)-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. The Zolgensma® drug product infringes the Asserted Patents by (i) using AskBio's self-

complementary rAAV vectors, which are covered by and based on the fundamental innovation of the Carter Patents, as well as (ii) using the formulation of the '542 Patent to store the rAAV vector particles to avoid harmful aggregation.

27. 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.

Patents-in-Suit

28. The '535 Patent, entitled "Metabolically Activated Recombinant Viral Vectors and Methods for the Preparation and Use," issued on July 22, 2003 to inventor Dr. Barrie J. Carter. The '535 Patent was originally assigned to Targeted Genetics Corporation, then was subsequently assigned to Genzyme Corporation. A true and correct copy of the '535 Patent is attached as Exhibit B.

29. The '535 Patent issued from U.S. Patent Application No. 09/634,126, which claims priority to U.S. Provisional Patent Application No. 60/160,080, which was filed on August 9, 1999.

30. The '535 Patent expired on August 8, 2020. It was valid and enforceable under United States Patent Laws during its term and when the infringement occurred.

31. The '717 Patent, entitled "Metabolically Activated Recombinant Viral Vectors and Methods for the Preparation and Use," issued on October 24, 2006 to inventor Dr. Barrie J. Carter. The '717 Patent issued from a continuation of the '535 Patent. The '717 Patent was originally assigned to Targeted Genetics Corporation, then was subsequently assigned to Genzyme Corporation. A true and correct copy of the '717 Patent is attached as Exhibit C.

32. The ’717 Patent expires on March 29, 2022. It has been valid and enforceable at all times since it issued, and remains valid and enforceable.

33. The ’888 Patent, entitled “Metabolically Activated Recombinant Viral Vectors and Methods for the Preparation and Use,” issued on August 31, 2010 to inventor Dr. Barrie J. Carter. The ’888 Patent issued from a continuation of the ’717 Patent. The ’888 Patent was originally assigned to Targeted Genetics Corporation, then was subsequently assigned to Genzyme Corporation. A true and correct copy of the ’888 Patent is attached as Exhibit D.

34. The ’888 Patent expired on August 8, 2020. It was valid and enforceable under United States Patent Laws during its term and when the infringement occurred.

35. The ’729 Patent, entitled “Metabolically Activated Recombinant Viral Vectors and Methods for the Preparation and Use,” issued on August 28, 2008 to inventor Dr. Barrie J. Carter. The ’729 Patent issued from a continuation of the ’888 Patent. The ’729 Patent was originally assigned to Targeted Genetics Corporation, then was subsequently assigned to Genzyme Corporation. A true and correct copy of the ’729 Patent is attached as Exhibit E.

36. The ’729 Patent expired on August 8, 2020. It was valid and enforceable under United States Patent Laws during its term and when the infringement occurred.

37. The ’054 Patent, entitled “Metabolically Activated Recombinant Viral Vectors and Methods for the Preparation and Use,” issued on January 10, 2012 to inventor Barrie J. Carter. The ’054 Patent issued from a continuation of the ’729 Patent. The ’054 Patent was originally assigned to Targeted Genetics Corporation, then was subsequently assigned to Genzyme Corporation. A true and correct copy of the ’054 Patent is attached as Exhibit F.

38. The ’054 Patent expired on August 8, 2020. It was valid and enforceable under United States Patent Laws during its term and when the infringement occurred.

39. On information and belief, Defendants had knowledge of the '535 Patent, the '717 Patent, the '888 Patent, '729 Patent, and the '054 Patent at least as early as when Novartis Gene Therapies, Inc. entered into the license agreement with AskBio.

40. The '542 Patent, entitled "Compositions and Methods to Prevent AAV Vector Aggregation," issued on June 9, 2015. The '542 Patent issued from U.S. Patent Application No. 12/661,553, which claims priority ultimately to U.S. Provisional Patent Application No. 60/575,997 filed on June 1, 2004 and U.S. Provisional Patent Application No. 60/639,222 filed on December 22, 2004.

41. The '542 Patent was originally assigned to Avigen Inc., then was subsequently assigned to Genzyme Corporation. A true and correct copy of the '542 Patent is attached as Exhibit G.

42. The '542 Patent expires on June 1, 2025. It has been valid and enforceable at all times since it issued, and remains valid and enforceable.

Count I: Infringement of U.S. Patent No. 6,596,535

43. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 42 above as though fully set forth herein.

44. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '535 Patent, including but not limited to claim 1, under 35 U.S.C. § 271(a).

45. Although the '535 Patent expired on August 8, 2020, prior to expiry Defendants infringed the '535 Patent in violation of 35 U.S.C. § 271(a) at least by making, using, and/or selling Zolgensma® in the United States.

46. On information and belief, Defendants' pre-expiration manufacture, use, and/or sale of Zolgensma® infringed at least claim 1 of the '535 Patent.

47. The '535 patent has one independent claim, claim 1. Claim 1 recites:

> A recombinant adeno-associated virus (rAAV) vector comprising a single-stranded heterologous nucleotide sequence comprising a region which forms intrastrand base pairs such that expression of a coding region of the heterologous sequence is enhanced relative to a second rAAV vector that lacks sufficient intrastrand base pairing to enhance said expression, wherein the region which forms intrastrand base pairs is in a coding region.

48. On information and belief, Zolgensma® contains a rAAV vector that comprises a coding region of the *SMN* gene (i.e., a heterologous sequence) that forms intrastrand base pairs by utilizing intrastrand base pairing vector technology to increase the efficacy of the drug. *See* Exhibit A ("11. Description" ("[Zolgensma®] is a recombinant self-complementary AAV9 containing a transgene encoding the human survival motor neuron (SMN) protein.")).

49. Plaintiffs have suffered damages as a result of Defendants' infringement of the '535 Patent.

50. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '535 Patent, Defendants knew or should know that their actions infringe the '535 Patent.

Count II: Infringement of U.S. Patent No. 7,125,717

51. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 50 above as though fully set forth herein.

52. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '717 Patent, including but not limited to claims 1 and 2, under 35 U.S.C. §§ 271(a) and/or (b).

53. On information and belief, Defendants' manufacture, use, and/or sale of Zolgensma® infringes at least claims 1 and 2 of the '717 Patent.

54. On information and belief, Defendants have induced infringement of the '717 Patent of at least claim 1 of the '717 Patent under 35 U.S.C. § 271(b). Defendants knew of the '717 Patent, and that their conduct and communications induces users of Zolgensma® to directly infringe the '717 Patent. For instance, by means of the Zolgensma® label provided by Defendants and through other communications, Defendants instruct, direct, and encourage users of Zolgensma® and others with respect to the use of Zolgensma® with the knowledge that such use according to the label infringed the '717 Patent, intending that physicians and/or health care providers in the United States performed the directly infringing activities. On information and belief, such conduct by Defendants was intended to cause, and actually resulted in, direct infringement in the United States.

55. The '717 patent has two independent claims, claim 1 and claim 2. Claim 1 recites:

> A method for introducing a polynucleotide into a cell, comprising contacting the cell essentially in the absence of an AAV helper virus with a recombinant adeno-associated virus (rAAV) particle comprising an rAAV vector under conditions that allow uptake of the rAAV vector, whereby the rAAV vector is introduced into the cell, wherein the rAAV vector comprises a single-stranded heterologous nucleotide sequence comprising a coding region which forms intrastrand base pairs such that expression of the coding region of the heterologous sequence is enhanced relative to a second rAAV vector that lacks sufficient intrastrand base pairing to enhance said expression, wherein the rAAV vector comprises one or more inverted terminal repeat (ITR) sequence flanking said heterologous sequence

56. Claim 2 recites:

> A method for expressing a polynucleotide coding region in a cell, comprising subjecting the cell to conditions which allow expression of the coding region, whereby the coding region is expressed, wherein the polynucleotide coding region is introduced into the cell by contacting the cell essentially in the absence of an AAV helper virus with an rAAV particle comprising an rAAV vector, wherein

> the rAAV vector comprises a single-stranded heterologous nucleotide sequence comprising the coding region which forms intrastrand base pairs such that expression of the coding region of the heterologous sequence is enhanced relative to a second rAAV vector that lacks sufficient intrastrand base pairing to enhance said expression, wherein the rAAV vector comprises one or more inverted terminal repeat (ITR) sequences flanking said heterologous sequence.

57. On information and belief, Zolgensma® contains a functional copy of the *SMN* gene (i.e., a heterologous sequence) packaged in rAAV9. On information and belief, Zolgensma® contains a rAAV vector that contains a coding region of the *SMN* gene that forms intrastrand base pairs by utilizing intrastrand base pairing vector technology to increase the efficacy of the drug. *See* Exhibit A ("11. Description."). On information and belief, Zolgensma® contains a rAAV vector that contains one or more ITR sequences flanking the *SMN* sequence.

58. On information and belief, when administered to a patient, Zolgensma® delivers a copy of the coding region of the *SMN* gene to a cell where the SMN protein is expressed. On information and belief, Zolgensma® is administered without a helper virus.

59. Plaintiffs have suffered damages as a result of Defendants' infringement of the '717 Patent and will continue to suffer damages as long as those infringing activities continue.

60. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '717 Patent, Defendants knew or should know that their actions infringe the '717 Patent.

Count III: Infringement of U.S. Patent No. 7,785,888

61. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 60 above as though fully set forth herein.

62. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '888 Patent, including but not limited to claim 1, under 35 U.S.C. § 271(a).

63. Although the '888 Patent expired on August 8, 2020, prior to expiry Defendants infringed the '888 Patent in violation of 35 U.S.C. § 271(a) at least by making, using, and/or selling Zolgensma® in the United States.

64. On information and belief, Defendants' pre-expiration manufacture, use, and/or sale of Zolgensma® infringed at least claim 1 of the '888 Patent.

65. The '888 patent has one independent claim, claim 1. Claim 1 recites:

> A recombinant adeno-associated virus (rAAV) preparation, which rAAV virus preparation is essentially free of helper virus, comprising an rAAV particle, wherein the rAAV particle comprises an rAAV genome, wherein the rAAV genome comprises a heterologous nucleotide sequence comprising a coding region and one or more inverted terminal repeat (ITR) sequences flanking said heterologous sequence, wherein the total amount of unique sequence present in the heterologous sequence is about one-half of the heterologous sequence and wherein the heterologous sequence forms intrastrand base pairs along most or all of its length such that expression of the coding region is enhanced relative to an rAAV vector that lacks sufficient intrastrand base pairing to enhance expression.

66. On information and belief, Zolgensma® contains a functional copy of the *SMN* gene (i.e., a heterologous sequence) packaged in AAV9. On information and belief, Zolgensma® contains a rAAV vector that contains a rAAV genome and a coding region of the *SMN* gene that forms intrastrand base pairs by utilizing intrastrand base pairing vector technology to increase the efficacy of the drug. *See* Exhibit A ("11. Description."). On information and belief, Zolgensma® contains a rAAV vector that contains one or more ITR sequences flanking the *SMN* sequence.

67. On information and belief, Zolgensma® does not contain a helper virus.

68. Plaintiffs have suffered damages as a result of Defendants' infringement of the '888 Patent.

69. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '888 Patent, Defendants knew or should know that their actions infringe the '888 Patent.

Count IV: Infringement of U.S. Patent No. 7,846,729

70. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 69 above as though fully set forth herein.

71. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '729 Patent, including but not limited to claim 1, under 35 U.S.C. § 271(a).

72. Although the '729 Patent expired on August 8, 2020, prior to expiry Defendants infringed the '729 Patent in violation of 35 U.S.C. § 271(a) at least by making, using, and/or selling Zolgensma® in the United States.

73. On information and belief, Defendants' pre-expiration manufacture, use, and/or sale of Zolgensma® infringed at least claim 1 of the '729 Patent.

74. The '729 patent has one independent claim, claim 1. Claim 1 recites:

> A method for preparing a recombinant adeno-associated virus (rAAV), the method comprising:
>
> 1) incubating a host cell under conditions that allow AAV replication and encapsidation, wherein said host cell comprises:
>
> (a) a rAAV vector comprising a heterologous nucleotide sequence and one or more AAV inverted terminal repeat (ITR) sequences flanking said heterologous sequence, wherein the vector is less than about 2.5 kb, and
>
> (b) AAV rep function, AAV cap function, and helper virus function for AAV; and
>
> 2) purifying rAAV particles produced from the host cell, wherein the rAAV particles comprise a rAAV genome which forms intrastrand base pairs along its length, such that expression of a coding region of the heterologous sequence is enhanced relative to a rAAV vector that lacks sufficient intrastrand base pairing to enhance said expression

75. On information and belief, Zolgensma® has been and is prepared using a host cell under conditions that allow AAV replication and encapsidation and then purifying the rAAV particles produced from the host cell to select for rAAV particles containing vectors encoding the *SMN* transgene.

76. On information and belief, Zolgensma® contains a functional copy of the *SMN* gene (i.e., a heterologous sequence) packaged in rAAV9. On information and belief, Zolgensma® contains a rAAV vector that contains a rAVV genome and a coding region of the *SMN* gene that forms intrastrand base pairs along its length by utilizing intrastrand base pairing vector technology to increase the efficacy of the drug. *See* Exhibit A ("11. Description."). On information and belief, Zolgensma® contains a rAAV vector that contains one or more ITR sequences flanking the *SMN* sequence.

77. On information and belief, Zolgensma® contains a rAAV vector that is less than about 2.5 kb.

78. Plaintiffs have suffered damages as a result of Defendants' infringement of the '729 Patent.

79. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '729 Patent, Defendants knew or should know that their actions infringe the '729 Patent.

Count V: Infringement of U.S. Patent No. 8,093,054

80. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 79 above as though fully set forth herein.

81. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '054 Patent, including but not limited to claims 1 and 19, under 35 U.S.C. §§ 271(a) and/or (b).

82. Although the '054 Patent expired on August 8, 2020, prior to expiry Defendants infringed the '054 Patent in violation of 35 U.S.C. § 271(a) at least by making, using, and/or selling Zolgensma® in the United States.

83. On information and belief, Defendants' pre-expiration manufacture, use, and/or sale of Zolgensma® infringed at least claims 1 and 19 of the '054 Patent.

84. On information and belief, Defendants have induced infringement prior to the expiry of the '054 Patent of at least claim 1 of the '054 Patent under 35 U.S.C. § 271(b). Defendants knew of the '054 Patent, and that their conduct and communications induced users of Zolgensma® to directly infringe the '054 Patent. For instance, by means of the Zolgensma® label provided by Defendants and through other communications, Defendants instructed, directed, and encouraged users of Zolgensma® and others with respect to the use of Zolgensma® with the knowledge that such use according to the label infringed the '054 Patent, intending that physicians and/or health care providers in the United States performed the directly infringing activities. On information and belief, such conduct by Defendants was intended to cause, and actually resulted in, direct infringement in the United States.

85. The '054 patent has two independent claims, claim 1 and claim 19. Claim 1 recites:

> A composition comprising a purified recombinant adeno-associated virus (rAAV) particle comprising an AAV capsid and a single-stranded rAAV vector genome, wherein the rAAV vector genome comprises in the 5′ to 3′ direction: a 5′ AAV inverted terminal repeat (ITR) sequence, a first heterologous nucleotide sequence, an internal AAV ITR sequence, a second heterologous nucleotide sequence, and a 3′ AAV ITR sequence, wherein the first heterologous nucleotide sequence can form intrastrand base pairs with the second nucleotide sequence along most or all of its length.

86. Claim 19 recites:

> A method of expressing a polynucleotide coding sequence in a cell, comprising subjecting the cell to conditions which allow expression of the coding sequence, wherein the coding sequence is introduced into the cell by contacting the cell essentially in the absence of an AAV helper virus with a composition comprising a purified recombinant adeno-associated virus (rAAV) particle, wherein the rAAV particle comprises an AAV capsid and a single-stranded rAAV vector genome, wherein the rAAV vector genome comprises in the 5′ to 3′ direction: a 5′ AAV inverted terminal repeat (ITR) sequence, a first heterologous nucleotide sequence, an internal AAV ITR sequence, a second heterologous nucleotide sequence, and a 3′ AAV ITR sequence, wherein the first heterologous nucleotide sequence can form intrastrand base pairs with the second nucleotide sequence along most or all of its length, and wherein the first or the second heterologous nucleotide comprises the coding sequence.

87. On information and belief, Zolgensma® contains a functional copy of the *SMN* gene (i.e., a heterologous sequence) packaged in rAAV9. On information and belief, Zolgensma® contains a single-stranded rAAV vector genome that contains a coding region of the *SMN* gene that forms intrastrand base pairs by utilizing intrastrand base pairing vector technology to increase the efficacy of the drug. *See* Exhibit A ("11. Description."). On information and belief, Zolgensma® contains an AAV capsid. On information and belief, Zolgensma® contains a rAAV vector that contains one or more ITR sequences flanking the *SMN* sequence.

88. On information and belief, Zolgensma® does not contain a helper virus.

89. On information and belief, when administered to a patient, Zolgensma® delivers a copy of the *SMN* gene to a motor neuron cell where the SMN protein is expressed.

90. Plaintiffs have suffered damages as a result of Defendants' infringement of the '054 Patent.

91. On information and belief, Defendants' infringement has been willful. Since having knowledge of the '054 Patent, Defendants knew or should know that their actions infringe the '054 Patent.

Count VI: Infringement of U.S. Patent No. 9,051,542

92. Plaintiffs repeat and reallege the allegations set forth in paragraphs 1 through 91 above as though fully set forth herein.

93. On information and belief, Defendants' commercial manufacture, importation, use, offer to sell, or sale of Zolgensma® infringes one or more claims of the '542 Patent, including but not limited to claim 1, under 35 U.S.C. § 271(a).

94. On information and belief, Defendants' manufacture, use, and/or sale of Zolgensma® infringes at least claim 1 of the '542 Patent.

95. The '542 Patent has one independent claim, claim 1. Claim 1 recites:

> A composition for the storage of purified, recombinant adeno-associated virus (AAV) vector particles, comprising:
>
> purified, recombinant AAV vector particles at a concentration exceeding 1×10^{13} vg/ml up to 6.4×10^{13} vg/ml;
>
> a pH buffer, wherein the pH of the composition is between 7.5 and 8.0; and
>
> excipients comprising one or more multivalent ions selected from the group consisting of citrate, sulfate, magnesium, and phosphate; wherein the ionic strength of the composition is greater than 200 mM, and wherein the purified AAV vector particles are stored in the composition without significant aggregation.

96. On information and belief, Zolgensma® is provided as a composition for the storage of purified, recombinant adeno-associated virus (AAV) vector particles having a formulation as recited in claim 1 of the '542 Patent. In particular, on information and belief, the Zolgensma® suspension contains purified, recombinant adeno-associated virus (AAV) vector particles in a concentration exceeding 1×10^{13} vg/ml up to 6.4×10^{13} vg/ml, a pH buffer, wherein the pH of the composition is between 7.5 and 8.0, and excipients comprising one or more multivalent ions selected from the group consisting of citrate, sulfate, magnesium, and phosphate, wherein the

ionic strength of the composition is greater than 200 mM. *See* Exhibit A ("11. Description," stating that "ZOLGENSMA has a nominal concentration of 2.0×10^{13} vg/mL. Each vial contains an extractable volume of not less than either 5.5 mL or 8.3 mL and the excipients 20 mM Tris (pH 8.0), 1 mM magnesium chloride ($MgCl_2$), 200 mM sodium chloride (NaCl) and 0.005% poloxamer 188. ZOLGENSMA is packaged as a sterile suspension and contains no preservative.").

97. On information and belief, the Zolgensma® suspension is stored without significant aggregation. *See* Exhibit A ("2.2 Preparation" stating, "When thawed, ZOLGENSMA is a clear to slightly opaque, colorless to faint white liquid, free of particles.").

98. Plaintiffs have suffered damages as a result of Defendants' infringement of the '542 Patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court:

A. Enter judgment that Defendants have infringed the '535, '717, '888, '729,'054, and '542 Patents.

B. Enter judgment that Defendants' infringement of the '535, '717, '888, '729, and '054 Patents 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 and 154(d);

D. Enter judgment that this case is exceptional and award Plaintiffs their reasonable attorneys' fees, costs, and expenses, under 35 U.S.C. § 285; and

E. 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)
4250 Lancaster Pike, Suite 200
Wilmington, DE 19085
(302) 225-0858
Email: dwilks@wilks.law
Email: sczerwonka@wilks.law

Attorneys for Plaintiffs Genzyme Corporation and Aventis Inc.

OF COUNSEL:

Paul H. Berghoff
Joshua R. Rich
Nicole E. Grimm
George T. Lyons, III
Bryan G. Helwig, Ph.D.
Alexandra E. MacKenzie
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 South Wacker Drive
Chicago, IL 60606
(312) 913-0001

February 23, 2022