IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., a Japanese company; Plaintiff, v. SAREPTA THERAPEUTICS, INC., a Delaware corporation Defendant.	)	CIVIL ACTION NO. 21-1015 (LPS)

SECOND AMENDED COMPLAINT FOR BREACH OF CONTRACT, DECLARATORY JUDGEMENT OF PATENT INVALIDITY, AND PATENT INFRINGEMENT

Nippon Shinyaku Co., Ltd. ("Nippon Shinyaku" or "Plaintiff") by and through its undersigned attorneys, alleges as follows for its Second Amended Complaint for Breach of Contract, Declaratory Judgment of Patent Invalidity, and Patent Infringement against Sarepta Therapeutics, Inc. ("Sarepta" or "Defendant"):

Nature of the Action

1. Nippon Shinyaku asserts a claim for breach of contract. This claim arises out of Sarepta's breach of its Mutual Confidentiality Agreement ("MCA," D.I. 2-1) with Nippon Shinyaku. Sarepta breached the MCA by filing seven petitions for *Inter Partes Review* (collectively, the "IPR Petitions") with the Patent Trial and Appeal Board ("PTAB") at the United States Patent and Trademark Office ("USPTO").[1] The IPR Petitions seek to invalidate U.S. Patent

[1] Sarepta's IPR Petitions were filed with the following case numbers: (i) IPR2021-01134; (ii) IPR2021-01135; (iii) IPR2021-01136; (iv) IPR2021-01137; (v) IPR2021-01138; (vi) IPR2021-01139; and (vii) IPR2021-01140.

Nos. 9,708,361 ("'361 Patent," D.I. 2-2); 10,385,092 ("'092 Patent," D.I. 2-3); 10,407,461 ("'461 Patent," D.I. 2-4); 10,487,106 ("'106 Patent," D.I. 2-5); 10,647,741 ("'741 Patent, D.I. 2-6); 10,662,217 ("'217 Patent, D.I. 2-7); and 10,683,322 ("'322 Patent," D.I. 2-8). Sarepta's filing of the IPR Petitions directly contravenes the MCA's forum selection clause, which requires that Sarepta and Nippon Shinyaku bring any such patent challenges in the United States District Court for the District of Delaware.

2. Nippon Shinyaku also asserts claims for declaratory judgment of invalidity of United States Patent Nos. 9,994,851 ("'851 Patent," D.I. 2-9), 10,227,590 ("'590 Patent," D.I. 2-10), and 10,266,827 ("'827 Patent," D.I. 2-11) (collectively, the "Western Australia Patents" or "UWA Patents"). Upon information and belief, Sarepta is the exclusive licensee with assertion rights for the UWA Patents.

3. Nippon Shinyaku further asserts claims for patent infringement of the '361 Patent, '092 Patent, '461 Patent, '106 Patent, '741 Patent, '217 Patent, and '322 Patent (collectively, the "NS Patents"). These claims arise out of Sarepta's manufacture, use, sale, offers to sell within the United States, and/or importation into the United States of its morpholino antisense oligomer ("ASO") that induces skipping of exon 53 of the human dystrophin gene to treat Duchenne Muscular Dystrophy ("DMD") and Sarepta's intentional encouragement of physicians to administer this ASO to patients. Sarepta developed this ASO under the names "SRP-4053" and "golodirsen" and markets it in the United States as VYONDYS 53.

Parties

4. Nippon Shinyaku is a Japanese company with a principal place of business at 14, Nishinosho-Monguchi-cho, Kisshoin, Minami-ku, Kyoto 601-8550, Japan.

5. Nippon Shinyaku is an innovative pharmaceutical company whose mission is to "help people lead healthier, happier lives." It accomplishes this mission by developing and supplying unique and high-quality therapies that are safe and highly effective relative to other drugs and that contribute to a better quality of life for patients.

6. Nippon Shinyaku not only serves general patient populations through its various drugs for urological diseases, hematology, gynecology, and otorhinolaryngology—but it also seeks to provide meaningful relief for patients suffering from rare, intractable diseases like DMD.

7. Upon information and belief, Sarepta is a Delaware corporation with its principal place of business at 215 First Street, Cambridge, Massachusetts 02142.

Jurisdiction and Venue

8. Nippon Shinyaku's claim for breach of contract arises under Delaware state law. This Court has subject matter jurisdiction over this breach of contract claim under 28 U.S.C. §§ 1332(a) and 1367(a).

9. Nippon Shinyaku's claims for declaratory judgment of invalidity of the UWA Patents arise under the Patent Laws of the United States, 35 U.S.C. §§ 1 et seq. and under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 et seq.

10. This Court has subject-matter jurisdiction over these claims under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

11. Nippon Shinyaku and Sarepta are direct competitors that each provide antisense oligonucleotide-based therapies for the treatment of DMD. Sarepta and Nippon Shinyaku are the only companies with FDA clearance to market oligonucleotide therapies that induce exon 53-skipping for the treatment of DMD for patients in need thereof. Sarepta's product is marketed

under the name VYONDYS 53, and Nippon Shinyaku's product is marketed under the name VILTEPSO®.

12. In 2013 and 2015, the University of Western Australia ("UWA") obtained two patents directed towards antisense oligonucleotide-based therapies for the treatment of DMD: U.S. Patent No. 8,455,636 ("the '636 Patent) (D.I. 39-1) and 9,024,007 ("the '007 Patent) (D.I. 39-2). Each of these patents' claims encompasses Sarepta's VYONDYS 53 but fails to encompass Nippon Shinyaku's VILTEPSO®.

13. On January 16, 2017, FDA granted Orphan Drug Designation to Nippon Shinyaku for its antisense oligonucleotide-based therapy that would eventually be approved and marketed under the name VILTEPSO®. D.I. 39-3. Subsequent to FDA granting this Orphan Drug Designation, applications for the three UWA Patents were filed with the United States Patent and Trademark Office ("USPTO"). These UWA Patents, unlike the '636 Patent and '007 Patent, included new claims aimed at capturing VILTEPSO®. Sarepta has listed the UWA Patents on its FDA Orange Book listing for VYONDYS 53. NDA applicants "shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). In the Orange Book, Sarepta lists a patent expiry date for the UWA Patents of June 28, 2025 but are seeking a significant patent term extension that would extend their expiry date at least with respect to claims covering VYONDYS 53®.

14. Sarepta and Nippon Shinyaku have engaged in non-confidential communications regarding the licensing of Serapta's UWA Patents. Sarepta has taken affirmative action toward Nippon Shinyaku's VILTEPSO® product.

15. After some initial discussion, a meeting occurred on or about January 13, 2020, during which Sarepta's VYONDYS 53 product and Nippon Shinyaku's VILTEPSO® product were discussed. The meeting was attended by at least Mr. Matthew Gall of Sarepta and Mr. Masaya Toda of Nippon Shinyaku. As a result of that January 13, 2020, meeting, the Parties agreed to engage in negotiations concerning the Parties' patent portfolios, including Sarepta's UWA Patents. Sarepta requested that further discussions be held under a confidentiality agreement, and Nippon Shinyaku understood that these discussions would include discussions of licensing Sarepta's UWA Patents to avoid litigation.

16. During the same timeframe and before January 28, 2020, Chris Verni, Sarepta's Chief IP counsel sought out Nippon Shinyaku's outside counsel while they were attending a conference for the Association of Corporate Patent Counsel. Mr. Verni raised concerns about the possibility of litigation between the Parties and encouraged discussions as a means to avoid litigation.

17. After June 1, 2021, Sarepta and Nippon Shinyaku were no longer engaged in confidential discussions relating to their respective patent portfolios or products. Sarepta had not granted a license or covenant not to sue to Nippon Shinyaku for the UWA Patents, and Nippon Shinyaku had not granted a license or covenant not to sue Sarepta to the NS Patents.

18. On July 6, 2021, Mr. Joe Zenkus, Senior Vice President at Sarepta, emailed Mr. Masaya Toda at Nippon Shinyaku regarding Sarepta's filing of the IPR Petitions to invalidate the NS Patents. D.I. 39-4. In his email, Mr. Zenkus notes that "Sarepta was compelled to file the IPRs against the seven patents that NS obtained in the US to seek to cover Vyondys 53 [the NS Patents]."

19. He further notes that "Sarepta is prepared to continue on with the IPRs and ***pursue other actions deemed necessary for it to protect its rights***." Mr. Zenkus' statement was neither an admission of liability nor the amount of liability as to the NS Patents, but rather a present threat that Sarepta will assert its UWA Patents against Nippon Shinyaku. This communication was not subject to any confidentiality obligation. Under these circumstances, and as a result of at least these communications, Nippon Shinyaku was and remains under a reasonable apprehension that Sarepta would file a lawsuit asserting the UWA Patents against Nippon Shinyaku's U.S. sales of its VILTEPSO® product and threatening Nippon Shinyaku's goal to serving DMD patients and growing its U.S. market for this product. Nippon Shinyaku contends that no license is required from Sarepta under the UWA Patents for its continued sale of VILTEPSO®, and Nippon Shinyaku seeks to be free of risk of a claim for damages or other remedies by Sarepta in the future. Thus, a controversy existed when Nippon filed its original complaint in this matter on July 13, 2021 and continues to exist between the parties as to the non-infringement and invalidity of the UWA Patents.[2]

20. On September 8, 2021, Nippon Shinyaku sent Sarepta a covenant not to sue Nippon Shinyaku for infringement of the UWA Patents due to Nippon Shinyaku's making, using, offering to sell, selling, and/or importing into the United States VILTEPSO® and requested that Sarepta

[2] In order to ensure that this case can promptly move forward (and eliminating another basis for Sarepta purportedly delaying this case), NS will proceed on the Claims noted above and reserves the right to plead the defense of non-infringement in response to a Sarepta claim of infringement.

immediately execute that agreement. Despite having adequate time to consider Nippon Shinyaku's offer, Sarepta has failed to respond or execute the convent not to sue.

21. Nippon Shinyaku's claims for patent infringement of the NS Patents arise under the Patent Laws of the United States, 35 U.S.C. §§ 1 et seq.

22. The amount in controversy exceeds $75,000, exclusive of interest and costs.

23. Upon information and belief, Sarepta markets and sells ASOs, including VYONDYS 53. Upon information and belief, Sarepta currently manufactures, sells and offers to sell VYONDYS 53 throughout the United States and in this District.

24. This Court has subject-matter jurisdiction over these claims for patent infringement under 28 U.S.C. §§ 1331 and 1338(a).

25. This Court has personal jurisdiction over Sarepta, a Delaware corporation, at least because Sarepta resides in this District and has consented to this Court's jurisdiction. D.I. 2-1, Section 10.

26. Venue is proper under 28 U.S.C. §§ 1391(b), 1391(c), and 1400(b) at least because Sarepta, a Delaware corporation, resides in this District and because Sarepta has consented to this venue. D.I. 2-1, Section 10.

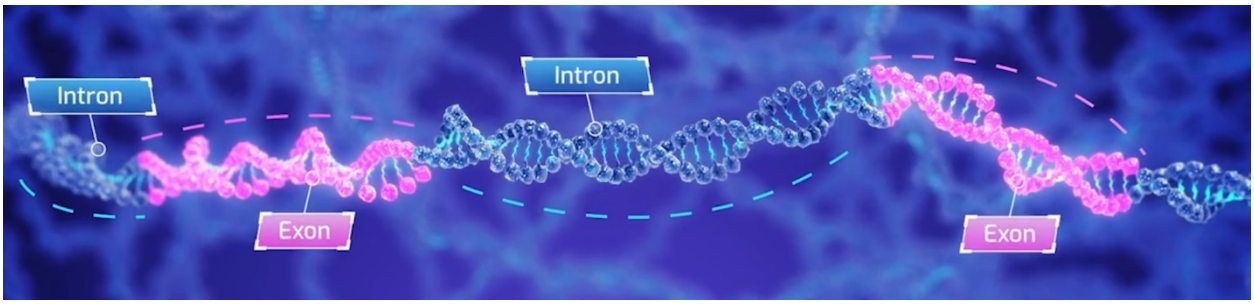
Duchenne Muscular Dystrophy

27. DMD is a severe X chromosome-linked genetic disorder that predominantly affects young boys. Approximately one in every 3,500 boys suffer from DMD, which is the most common form of hereditary progressive muscular dystrophy. Children with DMD suffer muscle weakness as early as age four and progressively lose muscle function and quality-of-life. By age twelve, DMD patients typically lose ambulatory function and are confined to wheelchairs. Body-wide muscle loss also contributes to numerous other health complications throughout patients' lives.

As a result of DMD-induced cardiac and/or respiratory deficiencies, most patients suffering from DMD do not live past their twenties.

28. DMD is caused by mutation(s) in the dystrophin gene, which codes for the dystrophin protein. The dystrophin protein contributes to cell membrane stability in muscle cells and makes muscle cells less fragile. In DMD patients, however, the mutated dystrophin gene causes significant under-expression of the dystrophin protein, leaving them with insufficient levels of dystrophin protein to maintain their muscle cells.

29. The dystrophin gene is long, spanning approximately 2.2 million nucleotide pairs and comprising 79 exons (regions of nucleotides that code for the 3,685 amino acids making up the dystrophin protein) interspersed with introns (regions that do not code for the dystrophin protein).



30. In a non-DMD patient, cells generally prepare dystrophin protein from the gene as follows:

> **Transcription:** The dystrophin gene (DNA) is transcribed into an RNA strand containing both exons and introns known as "pre-mRNA."
>
> **Splicing:** Cellular machinery removes intron sequences and "splices" the exons together to form mRNA.
>
> **Translation:** Cellular machinery "reads" the mRNA strand three nucleotides at a time to determine and assemble the amino acid sequence for dystrophin.

31. DMD typically results when a mutation shifts the amino acid reading frame, producing a non-functional dystrophin protein. As show below, even a single nucleotide deletion can alter how the cellular machinery reads the remainder of the mRNA sequence (and consequently how the cell assembles the dystrophin protein).

Original: ABC ABC ABC ABC ABC ABC

Mutation: ABA BCA BCA BCA BCA BCA

32. Mutations that preserve the original amino acid reading frame may produce a partially functional dystrophin protein with exon deletions. This typically causes a less-severe condition known as Becker Muscular Dystrophy ("BMD"). Like DMD, BMD patients suffer from muscle weakness and atrophy, but they experience milder and slower disease progression. Many BMD patients do not experience symptoms of disease onset until they are well into adulthood.

33. There is no cure for DMD. Care providers have traditionally prescribed corticosteroids to promote muscle strength and delay disease progression. Such treatment carries substantial risks of side-effects, including weight gain and weakened bones, and does not stop the progress of the disease.

Exon-Skipping Antisense Oligomers as a Therapeutic Option

34. Antisense oligomers ("ASOs") are short nucleic acid strands that modify splice patterns to address the genetic defects responsible for DMD. ASOs bind with particular nucleotide sequences in or near the exon of interest on the pre-mRNA strand. ASOs interfere with the ordinary splicing process, causing the cell to "skip" the mutated exon(s) when preparing mRNA.

35. By "skipping" the mutated exons, ASOs cause cells to prepare shorter-than-normal mRNA while preserving the original amino acid reading frame. As a result, patients' cells produce partially functional—rather than non-functional—protein. Applied to DMD, these treatments

effectively convert a DMD patient into a BMD patient, providing substantially better quality-of-life.

Nippon Shinyaku's Development of Exon 53 Skipping Oligomers

36. Recognizing the severe impact of DMD, Nippon Shinyaku began developing exon skipping therapies for DMD. Nippon Shinyaku focused first on therapies targeting exon 53, which would provide a treatment for approximately 8% of all DMD patients. Nippon Shinyaku ultimately determined that a 21 nucleobase (also call a 21mer) sequence targeted to the 36th to 56th nucleotides from the 5' end of exon 53 (H53_36-56) exhibited superior exon skipping.

37. On September 1, 2010, Nippon Shinyaku and National Center of Neurology and Psychiatry ("NCNP") filed Japanese Patent App. No. 2010-196032, which described their discoveries.

38. Nippon Shinyaku has since continued its development of the 21mer ASO—now known as VILTEPSO®—and secured approval in both Japan and the United States for the use of VILTEPSO® in treating DMD. While clinical trials are ongoing, initial results are promising. "[D]ystrophin levels increased, on average, from 0.6% of normal at baseline to 5.9% of normal at week 25."[3] And VILTEPSO® patients did not experience kidney toxicity, a side effect the United States Food & Drug Administration ("FDA") reported for other ASOs. *Id.*

[3] FOOD & DRUG ADMIN., *FDA Approves Targeted Treatment for Rare Duchenne Muscular Dystrophy Mutation*, (Aug. 12, 2020), https://www.fda.gov/news-events/press-announcements/fda-approves-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation (last accessed July 8, 2021).

The NS Patents-In-Suit

39. On July 18, 2017, the '361 Patent, entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '361 Patent is fully maintained, valid, and enforceable. A copy of the '361 Patent is found at D.I. 2-2.

40. On August 20, 2019, the '092 Patent, entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '092 Patent is fully maintained, valid, and enforceable. A copy of the '092 Patent is found at D.I. 2-3.

41. On September 10, 2019, the '461 Patent entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '461 Patent is fully maintained and valid and enforceable. A copy of the '461 Patent is found at D.I. 2-4.

42. On November 26, 2019, the '106 Patent entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '106 Patent is fully maintained and valid and enforceable. A copy of the '106 Patent is found at D.I. 2-5.

43. On May 12, 2020, the '741 Patent entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '741 Patent is fully maintained and valid and enforceable. A copy of the '741 Patent is found at D.I. 2-6.

44. On May 26, 2020, the '217 Patent entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '217 Patent is fully maintained and valid and enforceable. A copy of the '217 Patent is found at D.I. 2-7.

45. On June 16, 2020, the '322 Patent entitled "Antisense Nucleic Acids," issued to Nippon Shinyaku and NCNP as assignees with named inventors Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. The '322 Patent is fully maintained and valid and enforceable. A copy of the '322 Patent is found at D.I. 2-8.

46. By virtue of a license agreement with NCNP, Nippon Shinyaku holds the exclusive assertion rights for the NS Patents. Specifically, the License Agreement at Art. 3(2) (Third Party Patent Infringement Lawsuit) provides that (i) Nippon Shinyaku shall have an ***exclusive right*** to file suit against third party infringers of the NS Patents and (ii) NCNP has no rights whatsoever to initiate patent infringement suits based on the NS Patents against third party infringers. D.I. 39-5.

47. Because NCNP relinquished all rights to pursue infringement allegations relating to the NS Patents against third party infringers to Nippon Shinyaku, NCNP is not a required party under Fed. R. Civ. P. 19(a). As Nippon Shinyaku holds the exclusive right to bring infringement allegations against third party infringers for infringement of the NS Patents, the court can "accord complete relief among existing parties" without NCNP being a party to the litigation. *See* Fed. R. Civ. P. 19(a)(1)(A). Additionally, as NCNP retains no rights to assert patent infringement against third party infringers, there is no risk of Sarepta "incurring double, multiple, or otherwise inconsistent obligations" if NCNP is not a party to this litigation. *See* Fed. R. Civ. P. 19(a)(1)(B)(ii).

48. Additionally, even if NCNP is deemed a required party under Fed. R. Civ. P. 19(a), it would not be an indispensable party such that the court cannot in equity and good conscience proceed among the existing parties. *See* Fed. R. Civ. P. 19(b). As stated in paragraph 47, NCNP retains no rights to bring allegations of infringement of the NS Patents against third party infringers. Thus, there is no prejudice to NCNP by not being joined to this case nor is there prejudice to Sarepta in that it could be subjected to multiple infringement suits relating to the NS Patents.

The UWA Patents

49. On June 12, 2018, the ’851 Patent entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof” issued to the University of Western Australia (“UWA”) as assignees with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey. On information and belief, Sarepta holds exclusive assertion rights of the ’851 Patent.

50. On March 12, 2019, the ’590 Patent entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof” issued to UWA as assignees with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey. On information and belief, Sarepta holds exclusive assertion rights of the ’590 Patent.

51. On April 23, 2019, the ’827 Patent entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof” issued to The UWA as assignees with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey. On information and belief, Sarepta holds exclusive assertion rights of the ’827 Patent.

Sarepta's Infringing Product

52. Upon information and belief, Sarepta's product, VYONDYS 53, is a 25mer ASO that is 100% complementary, according to Watson-Crick base pairing, to the 36th to 60th nucleotides from the 5' end of exon 53 of human dystrophin pre-mRNA and hybridizes with the 36th to 60th nucleotides from the 5' end of exon 53 of human dystrophin pre-mRNA.[4]

53. Upon information and belief, VYONDYS 53 induces skipping of the 53rd exon in a human dystrophin pre-mRNA.

54. Upon information and belief, VYONDYS 53 is administered to patients and induces skipping of the 53rd exon of human dystrophin pre-mRNA in patients. Sarepta's label for VYONDYS 53 has encouraged—and continue to encourage—such use.

55. Upon information and belief, Sarepta copied VYONDYS 53 from Japanese Patent App. No. 2010-196032 and/or another related patent application.

56. Upon information and belief, since at least 2014, Sarepta actively researched and developed VYONDYS 53, including the development and approval of clinical trials.

57. On December 12, 2019, FDA announced it had granted accelerated approval to VYONDYS 53 for the treatment of DMD.[5]

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[4] *See, e.g.*, Highlights of Prescribing Information (Dec. 12, 2019) § 11, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211970s000lbl.pdf (last accessed July 8, 2021); Highlights of Prescribing Information (Feb. 11, 2021) § 11, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/211970s002lbl.pdf (last accessed July 8, 2021).

[5] FOOD & DRUG ADMIN., *FDA Grants Accelerated Approval to First Targeted Treatment for Rare Duchenne Muscular Dystrophy Mutation*, (Dec. 12, 2019), https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation (last accessed July 8, 2021).

58. On December 12, 2019, Sarepta announced that "[c]ommercial distribution of VYONDYS 53 in the U.S. will commence immediately."[6]

59. Upon information and belief, since at least December 2019, Sarepta has manufactured, offered for sale, and sold VYONDYS 53 in the United States for the treatment of DMD. Sarepta's Form 10-K Annual Report for 2020 describes VYONDYS 53 as a "commercial product" and states that VYONDYS 53 was "sold in 2020 and 2019."

60. Upon information and belief, since at least December 2019, Sarepta has encouraged physicians to treat DMD patients by administering VYONDYS 53 to induce skipping of the 53rd exon of human dystrophin pre-mRNA in patients, including through its labels for VYONDYS 53.

Sarepta's Breach of the MCA

61. Sarepta and Nippon Shinyaku entered into the MCA effective June 1, 2020. D.I. 2-1.

62. Under the MCA, Sarepta and Nippon Shinyaku each covenanted "for itself, its Affiliates and their respective Representatives" not to file "Potential Actions in the United States" during the "Covenant Term." *Id.* at Section 6.1.

63. Sarepta and Nippon Shinyaku also covenanted "that all Potential Actions arising under U.S. law relating to patent infringement or invalidity, and filed within two (2) years of the end of the Covenant Term, shall be filed in the United States District Court for the District of Delaware." *Id.* at Section 10.

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[6] Sarepta Therapeutics, *Sarepta Therapeutics Announces FDA Approval of VYONDYS 53™ (golodirsen) Injection for the Treatment of Duchenne Muscular Dystrophy (DMD) in Patients Amenable to Skipping Exon 53*, (Dec. 12, 2019), *available at* https://investorrelations.sarepta.com/static-files/15f0244f-6c99-42de-9919-30e801049ee0 (last accessed July 8, 2021).

64. The Agreement defines "Potential Actions" as "any patent or other intellectual property disputes between NS and Sarepta, or their Affiliates, other than the EP Oppositions or JP Actions, filed with a court or administrative agency prior to or after the Effective Date in the United States, Europe, Japan or other countries in connection with the Parties' development and commercialization of therapies for Duchenne Muscular Dystrophy." *Id.* at Section 1.

65. The Agreement defines the "Covenant Term" as "the time period commencing on the Effective Date and ending upon twenty (20) days after the earlier of: (i) expiration of the Term, or (ii) the effective date of termination." *Id.*; *see also id.* at Section 7 (defining "Term" as "one (1) year following the Effective Date"—i.e. through June 1, 2021—"or, if prior to such time, until one Party provides written notification of termination to the other Party").

66. Sarepta filed its seven IPR Petitions with the PTAB on June 21, 2021, seeking to invalidate all claims of the '361 Patent, the '092 Patent, the '461 Patent, the '106 Patent, the '741 Patent, the '217 Patent, and the '322 Patent.

CLAIM I
(Breach of Contract)

67. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

68. The MCA is a valid and enforceable contract between Nippon Shinyaku and Sarepta.

69. Section 10 of the MCA states, in relevant part:

> [A]ll Potential Actions arising under U.S. law relating to patent infringement or invalidity, and filed within two (2) years of the end of the Covenant Term, shall be filed in the United States District Court for the District of Delaware.[7]

[7] D.I. 2-1 at § 10.

70. The MCA defines "Potential Actions" as:

> [A]ny patent or other intellectual property disputes between NS [Nippon Shinyaku] and Sarepta, or their Affiliates, other than the EP Oppositions or JP Actions, filed with a court or administrative agency prior to or after the Effective Date in the United States, Europe, Japan or other countries in connection with the Parties' development and commercialization of therapies for Duchenne Muscular Dystrophy.[8]

71. On June 21, 2021, Sarepta filed the IPR Petitions before the PTAB challenging the validity of Nippon Shinyaku's '361 Patent, '092 Patent, '461 Patent, '106 Patent, '741 Patent, '217 Patent, and '322 Patent—each of which is in connection with Nippon Shinyaku's development and commercialization of therapies for DMD.

72. By filing these IPR Petitions before the PTAB, Sarepta breached Section 10 of the MCA.

73. This breach of Section 10 of the MCA resulted in damage to Nippon Shinyaku, as it deprived Nippon Shinyaku of its bargained-for choice of forum under the MCA. This deprivation of Nippon Shinyaku's bargained-for choice of forum under the MCA cannot be translated into a monetary amount and has irreparably harmed Nippon Shinyaku. Nippon Shinyaku will be further irreparably harmed if Sarepta is not enjoined from continuing with its IPR Petitions before the PTAB.

74. Nippon Shinyaku has no adequate remedy at law.

75. Sarepta has consented to "the issuance of an injunction and to the ordering of specific performance for any breach" of the MCA. D.I. 2-1, Section 11.

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[8] *Id*. at 2.

CLAIM II
(Declaratory Judgment of Invalidity of the UWA Patents)

76. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

77. Nippon Shinyaku and Sarepta are direct competitors that each provide antisense oligonucleotide-based therapies for the treatment of DMD. Sarepta and Nippon Shinyaku are the only companies with FDA clearance to market oligonucleotide therapies that induce exon 53-skipping for the treatment of DMD for patients in need thereof. Sarepta's product is marketed under the name VYONDYS 53, and Nippon Shinyaku's product is marketed under the name VILTEPSO®.

78. In 2013 and 2015, the UWA obtained two patents directed towards antisense oligonucleotide-based therapies for the treatment of DMD: the '636 Patent (D.I. 39-1) and the '007 Patent) (D.I. 39-2). Each of these patents' claims encompasses Sarepta's VYONDYS 53 but fails to encompass Nippon Shinyaku's VILTEPSO®.

79. On January 16, 2017, FDA granted Orphan Drug Designation to Nippon Shinyaku for its antisense oligonucleotide-based therapy that would eventually be approved and marketed under the name VILTEPSO®. D.I. 39-3. Subsequent to FDA granting this Orphan Drug Designation, applications for the three UWA Patents were filed with the United States Patent and Trademark Office ("USPTO"). These UWA Patents, unlike the '636 Patent and '007 Patent, included new claims aimed at capturing VILTEPSO®. Sarepta has listed the UWA Patents on its FDA Orange Book listing for VYONDYS 53. NDA applicants "shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner

engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). In the Orange Book, Sarepta lists a patent expiry date for the UWA Patents of June 28, 2025 but are seeking a significant patent term extension that would extend their expiry date at least with respect to claims covering VYONDYS 53®.

80. Sarepta and Nippon Shinyaku have engaged in non-confidential communications regarding the licensing of Serapta's UWA patents. Sarepta has taken affirmative action toward Nippon Shinyaku's VILTEPSO® product.

81. After some initial discussion, a meeting occurred on or about January 13, 2020, during which Sarepta's VYONDYS 53 product and Nippon Shinyaku's VILTEPSO® product were discussed. The meeting was attended by at least Mr. Matthew Gall of Sarepta and Mr. Masaya Toda of Nippon Shinyaku. As a result of that January 13, 2020, meeting, the Parties agreed to engage in negotiations concerning the Parties' patent portfolios, including Sarepta's UWA Patents. Sarepta requested that further discussions be held under a confidentiality agreement, and Nippon Shinyaku understood that these discussions would include discussions of licensing Sarepta's UWA Patents to avoid litigation.

82. During the same timeframe and before January 28, 2020, Chris Verni, Saretpa's Chief IP counsel sought out Nippon Shinyaku's outside counsel while they were attending a conference for the Association of Corporate Patent Counsel. Mr. Verni raised concerns about the possibility of litigation between the Parties and encouraged discussions as a means to avoid litigation.

83. After June 1, 2021 Sarepta and Nippon Shinyaku were no longer engaged in confidential discussions relating to their respective patent portfolios or products. Sarepta had not granted a license or covenant not to sue to Nippon Shinyaku for the UWA Patents, and Nippon Shinyaku had not granted a license or covenant not to sue Sarepta to the NS Patents.

84. On July 6, 2021, Mr. Joe Zenkus, Senior Vice President at Sarepta, emailed Mr. Masaya Toda at Nippon Shinyaku regarding Sarepta's filing of the IPR Petitions to invalidate the NS Patents. D.I. 39-4. In his email, Mr. Zenkus notes that "Sarepta was compelled to file the IPRs against the seven patents that NS obtained in the US to seek to cover Vyondys 53 [the NS Patents]."

85. He further notes that "Sarepta is prepared to continue on with the IPRs and ***pursue other actions deemed necessary for it to protect its rights***." Mr. Zenkus' statement was neither an admission of liability nor the amount of liability as to the NS Patents, but rather a present threat that Sarepta will assert its UWA Patents against Nippon Shinyaku. This communication was not subject to any confidentiality obligation. Under these circumstances, and as a result of at least these communications, Nippon Shinyaku was and remains under a reasonable apprehension that Sarepta would file a lawsuit asserting the UWA Patents against Nippon Shinyaku's U.S. sales of its VILTEPSO® product and threatening Nippon Shinyaku's goal to serving DMD patients and growing its U.S. market for this product. Nippon Shinyaku contends that no license is required from Sarepta under the UWA Patents for its continued sale of VILTEPSO®, and Nippon Shinyaku seeks to be free of risk of a claim for damages or other remedies by Sarepta in the future. Thus, a controversy existed when Nippon filed its original complaint in this matter on July 13, 2021 and continues to exist between the parties as to the invalidity of the UWA Patents.

86. On September 8, 2021, Nippon Shinyaku sent Sarepta a covenant not to sue Nippon Shinyaku for infringement of the UWA Patents due to Nippon Shinyaku's making, using, offering to sell, selling, and/or importing into the United States VILTEPSO® and requested that Sarepta immediately execute that agreement. Despite having adequate time to consider Nippon Shinyaku's offer, Sarepta has failed to respond or execute the convent not to sue.

87. The claims of the UWA Patents are invalid for failing to comply with the conditions and requirements of the patent laws of the United States, including, specifically and without limitation, 35 U.S.C. §§ 102, 103, and 112, and the rules, regulations, and laws pertaining thereto.

88. For example, the UWA Patents are invalid under 35 U.S.C. § 103 in light of at least the following prior art, either alone or in combination:

U.S. Patent No. 6,653,467 B1 to Matsuo;

PCT Pub. No. WO 2002/024906 A1 to Van Ommen et al.;

PCT Pub. No. WO 2004/083432 A1 to Van Ommen et al.;

European Patent App. No. 1 568 769 A1 to Matsuo;

Errington, et al., 5 J. GENE MED. 518 (2003);

Morita et al., 11 BIORGANIC & MED. CHEM. 2211 (2003);

Summerton, 10 LTRS. IN PEPTIDE SCI. 215 (2003);

Summerton & Weller, 7 ANTISENSE & NUCLEIC ACID DRUG DEV. 187 (1997).

89. The UWA Patents are also invalid under the written description requirement of 35 U.S.C. § 112. For example, the inventors of the UWA Patents possessed, at most, only a very small number of ASOs, which are reported to display only a minimal amount of exon-skipping activity and none that meet each element for any independent claim. Thus, the ASOs within the inventors' possession are insufficient to support the broad genus of the claims.

90. The UWA Patents are also invalid under the enablement requirement of 35 U.S.C. § 112. For example, the UWA Patents do not reasonably inform a person of skill in the art how to determine whether a given ASO of "20 to 31 bases" with "at least 12 consecutive bases of . . . SEQ ID NO: 195" induces skipping of exon 53 and required undue experimentation, among other things, in order to practice the full scope of the claimed inventions.

91. The UWA Patents are further invalid under the indefiniteness requirement of 35 U.S.C. § 112.

CLAIM III
(Infringement of the '361 Patent)

92. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

93. Claim 1 of the '361 Patent claims:

> 1. An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of the nucleotide sequence of SEQ ID NO: 57, wherein the antisense oligomer is an oligonucleotide in which the sugar moiety and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer.

94. "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11. "Golodirsen contains 25 linked subunits." *Id.*

95. "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1.

96. "The sequence of bases from the 5' end to 3' end [of golodirsen] is GTTGCCTCCGGTTCTGAAGGTGTTC." *Id.*

97. VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the ’361 Patent.

98. On information and belief, Sarepta has infringed the ’361 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the ’ 361 Patent in violation of 35 U.S.C. § 271(a).

99. VYONDYS 53 is indicated “for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.” Highlights of Prescribing Information (Dec. 12, 2019) § 1. As such, VYONDYS 53 is not suitable for substantial non-infringing uses.

100. On information and belief, Sarepta has contributorily infringed the ’ 361 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the ’ 361 Patent in violation of 35 U.S.C. § 271(c).

101. Sarepta’s labels for VYONDYS 53 encourage physicians and patients to use VYONDYS 53 to treat “Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.” Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1.

102. On information and belief, Sarepta has induced infringement of the ’ 361 Patent by encouraging others to use VYONDYS 53 in the United States before the expiration of the ’ 361 Patent in violation of 35 U.S.C. § 271(b).

103. On information and belief, Sarepta’s infringement of the ’361 Patent has been willful. Sarepta had knowledge of the ’361 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the ’361 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

104. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285

CLAIM IV
(Infringement of the '092 Patent)

105. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

106. Claim 1 of the '092 Patent claims:

> 1. A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer that causes skipping of the 53rd exon in a human dystrophin pre-mRNA, consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in said human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, and wherein said PMO antisense oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing under physiological conditions.

107. "Golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass." Highlights of Prescribing Information (Dec. 12, 2019) § 11. "Golodirsen contains 25 linked subunits." *Id.*

108. "The sequence of bases from the 5' end to 3' end [of golodirsen] is GTTGCCTCCGGTTCTGAAGGTGTTC." *Id.*

109. The sequence 5'–GTTGCCTCCGGTTCTGAAGGTGTTC–3' is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in human dystrophin pre-mRNA that consists of a nucleotide sequence corresponding to SEQ ID NO: 1:

Positions 36 to 60 form the 5' end of SEQ ID No. 1 (shown 3' to 5')																										
3'	**C**	**A**	**A**	**C**	**G**	**G**	**A**	**G**	**G**	**C**	**C**	**A**	**A**	**G**	**A**	**C**	**T**	**T**	**C**	**C**	**A**	**C**	**A**	**A**	**G**	**5'**
5'	**G**	**T**	**T**	**G**	**C**	**C**	**T**	**C**	**C**	**G**	**G**	**T**	**T**	**C**	**T**	**G**	**A**	**A**	**G**	**G**	**T**	**G**	**T**	**T**	**C**	**3'**
Golodirsen (shown 5' to 3')																										

110. "Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1.

111. VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '092 Patent.

112. On information and belief, Sarepta has infringed the '092 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the '092 Patent in violation of 35 U.S.C. § 271(a).

113. VYONDYS 53 is indicated "for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1. As such, VYONDYS 53 is not suitable for substantial non-infringing uses.

114. On information and belief, Sarepta has contributorily infringed the '092 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the '092 Patent in violation of 35 U.S.C. § 271(c).

115. Sarepta's labels for VYONDYS 53 encourage physicians and patients to use VYONDYS 53 to treat "Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1.

116. On information and belief, Sarepta has induced infringement of the '092 Patent by encouraging others to use VYONDYS 53 in the United States before the expiration of the '092 Patent in violation of 35 U.S.C. § 271(b).

117. On information and belief, Sarepta's infringement of the '092 Patent has been willful. Sarepta had knowledge of the '092 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the '092 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

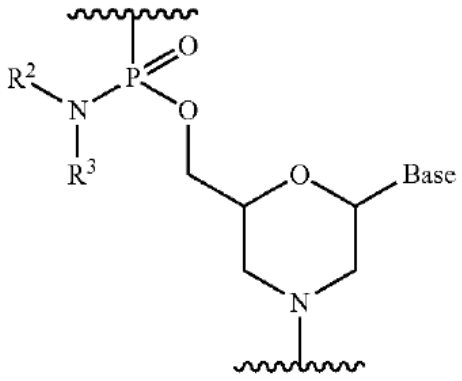
118. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

CLAIM V
(Infringement of the '461 Patent)

119. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

120. Claim 1 of the '461 Patent claims:

> 1. A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer that causes skipping of the 53rd exon in a human dystrophin pre-mRNA, consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124) of said human dystrophin pre-mRNA, wherein said PMO antisense oligomer hybridizes to said target sequence with Watson-Crick base pairing under physiological conditions, wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula:

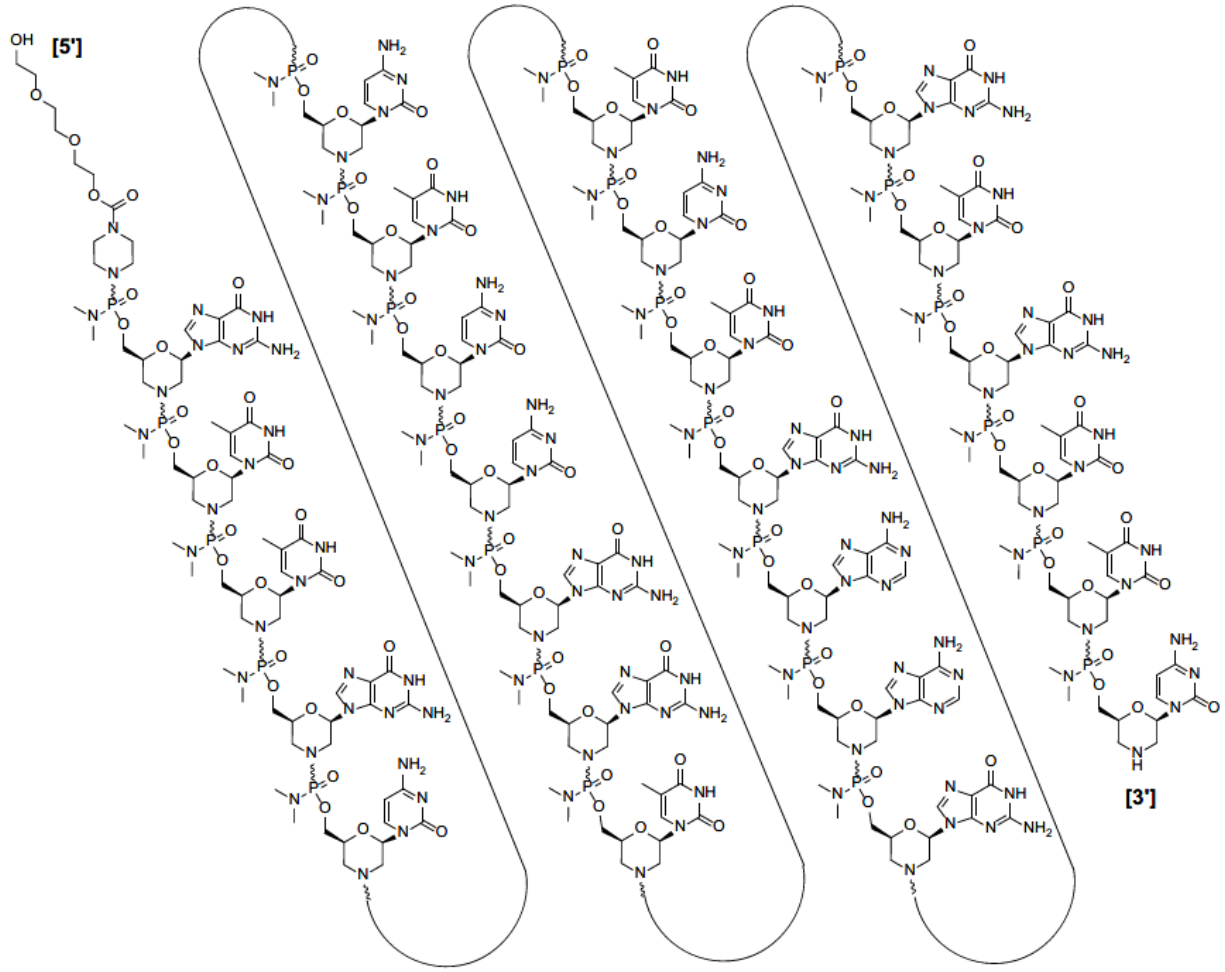


> wherein each of R^2 and R^3 represents a methyl; and wherein Base is a nucleobase selected from the group consisting of uracil, cytosine, thymine, adenine, and guanine.

121. The sequence 5'–GTTGCCTCCGGTTCTGAAGGTGTTC–3' is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124):

SEQ ID No. 124 (shown 3' to 5')																									
3'	**C**	**A**	**A**	**C**	**G**	**G**	**A**	**G**	**G**	**C**	**C**	**A**	**A**	**G**	**A**	**C**	**U**	**U**	**C**	**C**	**A**	**C**	**A**	**A**	**G**	**5'**
5'	**G**	**T**	**T**	**G**	**C**	**C**	**T**	**C**	**C**	**G**	**G**	**T**	**T**	**C**	**T**	**G**	**A**	**A**	**G**	**G**	**T**	**G**	**T**	**T**	**C**	**3'**
Golodirsen (shown 5' to 3')																									

122. The structure of golodirsen is:



Highlights of Prescribing Information (Dec. 12, 2019) § 11. As shown above, each monomer of golodirsen has methyl groups at the locations corresponding to R^2 and R^3 and a Base that is cytosine, thymine, adenine, or guanine.

123. As discussed above, VYONDYS 53 meets the remaining elements of claim 1 of the '461 Patent. VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '461 Patent.

124. On information and belief, Sarepta has infringed the ’461 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the ’461 Patent in violation of 35 U.S.C. § 271(a).

125. On information and belief, Sarepta has contributorily infringed the ’092 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the ’461 Patent in violation of 35 U.S.C. § 271(c).

126. On information and belief, Sarepta has induced infringement of the ’461 Patent by encouraging others to use VYONDYS 53 in the United States before the expiration of the ’461 Patent in violation of 35 U.S.C. § 271(b).

127. On information and belief, Sarepta’s infringement of the ’461 Patent has been willful. Sarepta had knowledge of the ’461 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the ’461 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

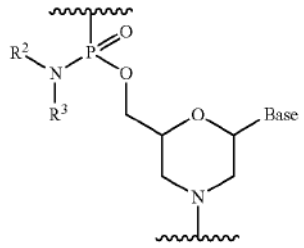
128. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys’ fees under 35 U.S.C. § 285.

CLAIM VI
(Infringement of the ’106 Patent)

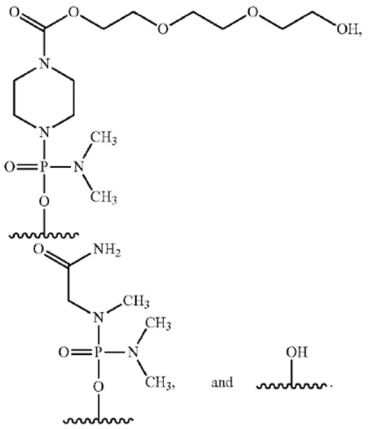
129. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

130. Claim 1 of the ’106 Patent claims:

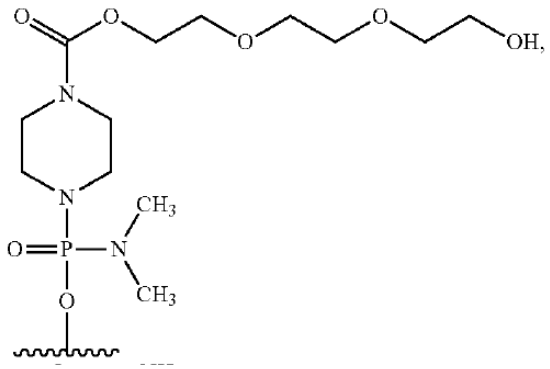
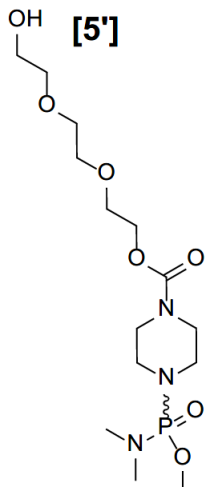
> 1. A phosphorodiamidate morpholino oligomer (PMO) consisting of a 25-mer antisense oligomer that is 100% complementary, according to Watson-Crick base pairing, to the 36th to the 60th nucleotides from the 5’ end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein each phosphorodiamidate morpholino monomer of said PMO has the formula:



wherein each of R^2 and R^3 represents a methyl; and wherein Base is a nucleobase selected from the group consisting of cytosine, thymine, adenine, and guanine; and wherein the 5' end of said PMO has a formula selected from the group consisting of:



131. The 5’ end of golodirsen has at least the claimed formula shown below:

 **Claim 1**	 **Golodirsen**

132. As discussed above, VYONDYS 53 meets the remaining elements of claim 1 of the '106 Patent. VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '106 Patent.

133. On information and belief, Sarepta has infringed the '106 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the '106 Patent in violation of 35 U.S.C. § 271(a).

134. On information and belief, Sarepta has contributorily infringed the '092 Patent by engaging in the commercial manufacture, use, offer to sell, sale, and/or importation into the United States of VYONDYS 53 before the expiration of the '106 Patent in violation of 35 U.S.C. § 271(c).

135. On information and belief, Sarepta has induced infringement of the '106 Patent by encouraging others to use VYONDYS 53 in the United States before the expiration of the '106 Patent in violation of 35 U.S.C. § 271(b).

136. On information and belief, Sarepta's infringement of the '106 Patent has been willful. Sarepta had knowledge of the '106 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the '106 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

137. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

CLAIM VII
(Infringement of the '741 Patent)

138. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

139. Claim 1 of the '741 Patent claims:

> 1. A method comprising administering to a patient with DMD an antisense phosphorodiamidate morpholino oligomer (PMO) consisting of a 25-mer oligomer

> that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, and wherein skipping of the 53rd exon is induced in said patient.

140. Sarepta's label for VYONDYS 53 encourage physicians to administer VYONDYS 53 to treat "Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1.

141. This administration of VYONDYS 53 "result[s] in exclusion of this exon [exon 53 of dystrophin pre-mRNA] during mRNA processing in patients." Highlights of Prescribing Information (Dec. 12, 2019) § 12.1; Highlights of Prescribing Information (Feb. 11, 2021) § 12.1.

142. As discussed above, VYONDYS 53 meets the remaining elements of claim 1 of the '741 Patent. This use of VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '741 Patent.

143. On information and belief, Sarepta has induced infringement of the '741 Patent by engaging in the commercial manufacture, use, offer to sell, sale, or importation into the United States of VYONDYS 53 for the purpose of administration to DMD patients and encouraging others to use the claimed methods in the United States before the expiration of the '741 Patent in violation of 35 U.S.C. § 271(b).

144. On information and belief, Sarepta's infringement of the '741 Patent has been willful. Sarepta had knowledge of the '741 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the '741 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

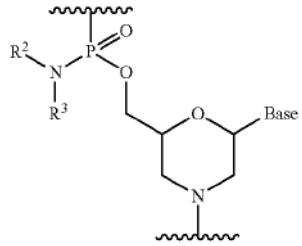
145. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

CLAIM VIII
(Infringement of the '217 Patent)

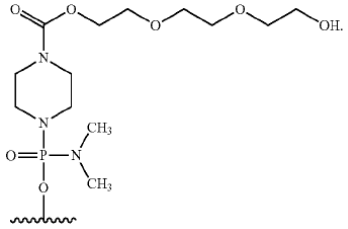
146. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

147. Claim 1 of the '217 Patent claims:

> 1. A method of treating a DMD patient comprising intravenously administering to said patient an oligomer comprising:
> a) a phosphorodiamidate morpholino oligomer (PMO) that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, wherein the phosphorodiamidate morpholino monomers of said PMO have the formula:



> wherein each of R^2 and R^3 represents a methyl; and wherein Base is a nucleobase selected from the group consisting of cytosine, thymine, adenine, and guanine; and
> b) a group at the 5' end of said PMO with the formula:



148. Sarepta's label for VYONDYS 53 encourage physicians to administer VYONDYS 53 to treat "Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of

the DMD gene that is amenable to exon 53 skipping." Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1.

149. Sarepta's label for VYONDYS 53 specifically instructs physicians that "VYONDYS 53 is administered via intravenous infusion." Highlights of Prescribing Information (Dec. 12, 2019) § 2.4; Highlights of Prescribing Information (Feb. 11, 2021) § 2.4.

150. As discussed above, VYONDYS meets the remaining elements of claim 1 of the '217 Patent. This use of VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '217 Patent.

151. On information and belief, Sarepta has induced infringement of the '217 Patent by engaging in the commercial manufacture, use, offer to sell, sale, or importation into the United States of VYONDYS 53 for the purpose of administration to DMD patients and encouraging others to use the claimed methods in the United States before the expiration of the '217 Patent in violation of 35 U.S.C. § 271(b).

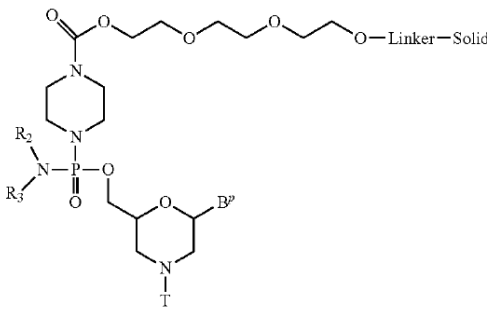
152. On information and belief, Sarepta's infringement of the '217 Patent has been willful. Sarepta had knowledge of the '217 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the '217 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

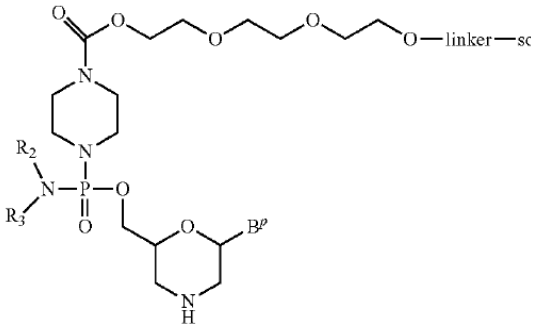
153. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

CLAIM IX
(Infringement of the '322 Patent)

154. Nippon Shinyaku realleges and incorporates by reference the allegations set forth in the preceding paragraphs as if fully set forth herein.

155. On information and belief, Sarepta's manufacturing process for VYONDYS 53 includes (i) reacting the compound shown below left with an acid to form the compound shown below right; and then (ii) reacting the compound shown below right with a morpholino monomer in the presence of a base and a solvent.

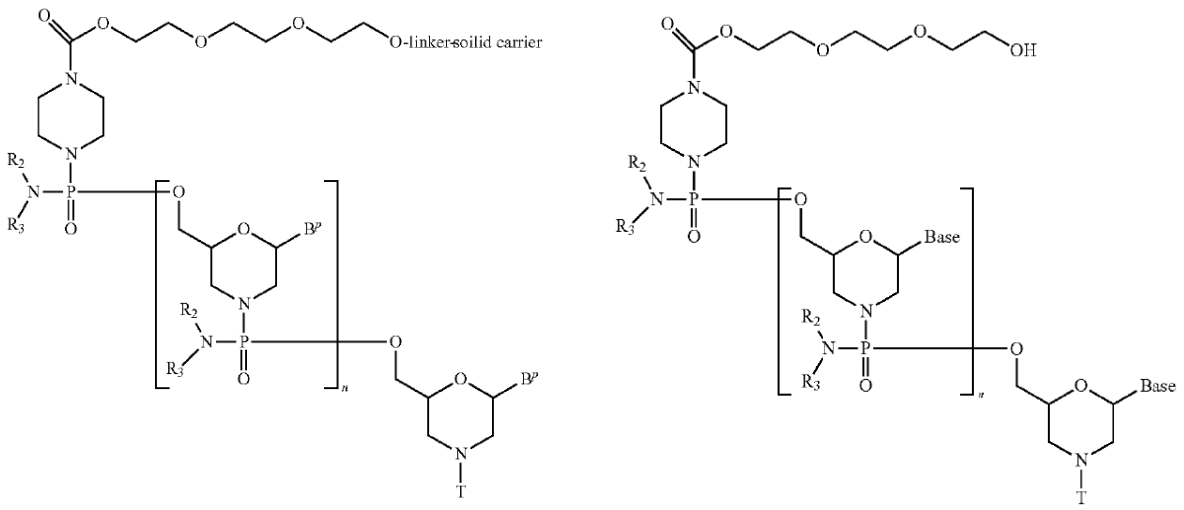




wherein T represents trityl, monomethoxytrityl, or
thoxytrityl; wherein each of R^2 and R^3 repres
methyl; and wherein B^P is a protected Base,

156. On information and belief, Sarepta's manufacturing process for VYONDYS 53 includes iteratively reacting the resultant compound first with an acid and then second with a morpholino monomer in the presence of a base and a solvent to add phosphorodiamidate morpholino monomers to the compound.

157. On information and belief, this iterative process results in the compound shown below left, which Sarepta reacts with a deprotecting agent to form the compound shown below right:



158. On information and belief, Sarepta's manufacturing process for VYONDYS 53 includes reacting the compound shown above right with an acid to form a phosphorodiamidate morpholino oligomer.

159. On information and belief, Sarepta's manufacturing process for VYONDYS 53 satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '322 Patent.

160. On information and belief, Sarepta has infringed the '322 Patent by engaging in the commercial manufacture, use, offer to sell, sale, or importation into the United States of VYONDYS 53 before the expiration of the '322 Patent in violation of 35 U.S.C. § 271(a) and (g).

161. As discussed above, VYONDYS meets the remaining elements of claim 1 of the '322 Patent. This use of VYONDYS 53 thus satisfies each element and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '322 Patent.

162. On information and belief, Sarepta has induced and/or contributed to infringement of the '322 Patent by engaging in the commercial manufacture, use, offer to sell, sale, or importation into the United States of VYONDYS 53 for the purpose of administration to DMD

patients and encouraging others to use the claimed methods in the United States before the expiration of the '322 Patent in violation of 35 U.S.C. § 271(b).

163. On information and belief, Sarepta's infringement of the '322 Patent has been willful. Sarepta had knowledge of the '322 Patent. Despite this knowledge, Sarepta continues to knowingly, willfully, deliberately, maliciously, and in bad faith infringe the '322 Patent, and, in doing so, knew or should have known that its conduct amounted to infringement.

164. This case is exceptional, and Nippon Shinyaku is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Nippon Shinyaku prays for judgment against Defendant Sarepta, respectfully requests the following relief:

1. A judgment that Sarepta has breached the MCA, including by having breached its obligations under Section 10;

2. A declaration of Sarepta's obligations under Section 10 of the MCA;

3. An order of specific performance of Sarepta's obligations under Section 10 of the MCA, including preliminary and permanent injunctions enjoining Sarepta, and its officers, agents, servants, and employees, and those persons acting in active concert or participation with all or any of them, from breaching its obligations under the MCA, and requiring Sarepta and said individuals to seek withdrawal and dismissal at the PTAB of the IPR Petitions;

4. An award of all legal fees and costs, including attorneys' fees, that Nippon Shinyaku incurs to prepare for and conduct its breach of contract action against Sarepta, as well as all legal fees and costs, including attorneys' fees, that Nippon Shinyaku incurs to oppose Sarepta's challenges before the PTAB;

5. A judgment that the UWA Patents are invalid;

6. A judgment that Sarepta has been and will continue infringing each of the NS Patents;

7. A judgment that Sarepta's infringement was willful and trebling any damages found or assessed;

8. To the extent that Sarepta has or will commercially manufacture, use, offer to sell, or sell VYONDYS 53 within the United States, or import VYONDYS 53 into the United States, prior to the expiration of the NS Patents, including any extensions, a judgment awarding Nippon Shinyaku monetary relief together with interest;

9. A judgment that this is an exceptional case and that Nippon Shinyaku be awarded its attorneys' fees incurred in this action pursuant to 35 U.S.C. § 285;

10. Costs and expenses in this action; and

11. Such other and further relief as the Court deems just and appropriate.

DEMAND FOR A JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(c), Nippon Shinyaku demands a jury trial solely regarding claims II-IX of the instant Amended Complaint.

Dated: January 14, 2022

Respectfully submitted,

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