IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

EXELA PHARMA SCIENCES, LLC, Plaintiff, v. NIVAGEN PHARMACEUTICALS, INC., Defendant.	Civil Action No . _____ **JURY TRIAL DEMANDED**

COMPLAINT

Plaintiff Exela Pharma Sciences, LLC ("Plaintiff" or "Exela") by its attorneys, hereby alleges as follows:

NATURE OF ACTION

1. This is an action for infringement of U.S. Patent No. 10,583,155 ("the '155 patent") and U.S. Patent No. 11,510,941 ("the '941 patent") arising under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.*, including §§ 271(a)-(c) and (e), against Defendant Nivagen Pharmaceuticals, Inc. and for a declaratory judgment of infringement of the '155 and '941 patents under 28 U.S.C. §§ 2201 and 2202 and 35 U.S.C. §§ 271(a)-(c).

THE PARTIES

2. Plaintiff Exela Pharma Sciences, LLC ("Exela" or "Plaintiff") is a company existing under the laws of the state of Delaware and having a principal place of business at 1245 Blowing Rock Blvd., Lenoir, NC 28645.

3. On information and belief, Defendant Nivagen Pharmaceuticals, Inc. ("Nivagen" or "Defendant") is a corporation organized and existing under the law of the State of Delaware, having a principal place of business at 3050 Fite Circle, Suite 100, Sacramento, CA 95827.

JURISDICTION AND VENUE

4. This Court has subject matter jurisdiction over the action under 28 U.S.C. §§ 1331 and 1338(a) because the action concerns a federal question arising under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq*.

5. This Court has personal jurisdiction over Nivagen Pharmaceuticals, Inc. because it is incorporated in Delaware and thus is present in and resides in this District, and because Nivagen is doing business in this District and thus has purposefully availed itself to the privileges of conducting business in Delaware. On information and belief, Harvard Business Services, Inc., 16192 Coastal Highway, Lewes, Delaware, is Nivagen's registered agent in Delaware and is authorized to accept service on Nivagen's behalf.

6. Venue is proper in this District pursuant to 28 U.S.C. § 1400(b) and § 1391 because Nivagen Pharmaceuticals, Inc. is incorporated in Delaware and thus resides in this District.

FACTUAL BACKGROUND

A. The Development and FDA Approval of Exela's ELCYS® L-Cysteine Product

7. Exela is a relatively small but fast-growing specialty pharmaceutical company focused on developing, manufacturing, and marketing injectable products.

8. L-cysteine is an amino acid that is important for human life. While healthy adults can naturally synthesize small amounts, high-risk patients such as preterm and/or low birth weight infants and patients with severe liver disease require L-cysteine supplementation by parenteral administration (i.e., injection or intravenous infusion). For these patients, L-cysteine is administered as a component of a nutritional supplement regimen referred to as "total parenteral nutrition" (TPN).

9. At the time Exela began developing its L-cysteine product, there was no FDA-approved intravenous L-cysteine hydrochloride product on the market in the United States. However, multiple unapproved and compounded L-cysteine products were on the market during that time that were used in TPN regimens. One significant drawback of such L-cysteine products is that they were known to contain high amounts of aluminum, labeled as containing up to 5,000 mcg/L.

10. TPN admixtures even without L-cysteine were also known to contain high amounts of aluminum, and aluminum toxicity from their use had been reported. Aluminum toxicity can cause serious health problems including dementia, impaired neurologic development, Alzheimer's disease, metabolic bone disease (including impaired bone growth, growth failure, bone pain, muscle weakness, nonhealing fractures, and premature osteoporosis), encephalopathy, and cholestasis (liver disease), among others.

11. In 2000, FDA issued regulations requiring manufacturers to reduce aluminum levels of parenteral products. Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition, 65 Fed. Reg. 4103 (Jan. 26, 2000). That regulation became final in 2004. Amendment of Regulations on Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition; Delay of Effective Date, 68 Fed. Reg. 32,979 (June 3, 2003). It requires manufacturers of TPN components to include the following warning on their product labeling: "Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 [micro]g/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity." Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition, 65 Fed. Reg. 4103, 4111 (Jan. 26, 2000). These regulations are codified at 21 C.F.R. § 201.323.

12. In April of 2019, after extensive effort, research, and development, including substantial work to achieve the ≤ 145 mcg/L aluminum level FDA mandated for the product, [Exhibit A (8/4/2017 FDA Letter)], Exela secured the first FDA approval for an injectable L-cysteine hydrochloride product containing low aluminum levels, finally fulfilling a long-felt need for such a low-aluminum injectable cysteine product.

13. Exela is the holder of approved New Drug Application ("NDA") No. 210660, approved under § 505(b)(2) of the Federal Food, Drug and Cosmetic Act, for a 5% cysteine hydrochloride injection, sold under the brand name ELCYS®.

14. The Reference Listed Drug ("RLD") for ELCYS® is a 7.25% cysteine hydrochloride product from Hospira that was approved under NDA No. 019523 ("Hospira Cysteine Hydrochloride Product") in 1986. This product was never commercially manufactured or marketed, and the NDA was ultimately withdrawn from approval in 2006. 75 Fed. Reg. 31790-91 (June 4, 2010).

15. Exela's ELCYS® product is labeled to contain no more than 120 micrograms/liter ("mcg/L," "µg/L" or, more commonly, parts per billion or ppb) of aluminum throughout the shelf life of the product, and is the only FDA approved L-cysteine product available on the market today. [Exhibit B (ELCYS® Label), § 11.]

16. Exela's ELCYS® product "is a sterile, nonpyrogenic solution for intravenous use. Each 10 mL of ELCYS contains 500 mg of cysteine hydrochloride, USP (equivalent of 345 mg of cysteine) in water for injection." [*Id.* at § 11.] The chemical name of L-cysteine hydrochloride is L-cysteine hydrochloride monohydrate. [*Id.*]

17. Exela's ELCYS® product has a pH in the range of 1.0 to 2.5. [*Id.*]

18. The FDA approved ELCYS® with a specification limiting the total impurities in the product, including pyruvic acid and cystine, both of which are observed as degradation products of L-cysteine, to no more than 2.0%.

19. The FDA approved ELCYS® with a specification for visual particulate matter of "essentially free of visible particulate matter." Exela's ELCYS® product met that specification throughout 24 months of stability testing. Accordingly, Exela's ELCYS® product remains free of visually detectable particulate matter for at least 24 months from the time of manufacture of the solution. Twenty-four months from the time of manufacture of the solution is the FDA-approved shelf-life of ELCYS®.

20. The FDA-approved labeling for Exela's ELCYS® product instructs healthcare providers that "ELCYS is indicated for use as an additive to amino acid solutions to meet the nutritional requirements of newborn infants requiring total parenteral nutrition (TPN) and of adult and pediatric patients with severe liver disease who may have impaired enzymatic processes and require TPN. It can also be added to amino acid solutions to provide a more complete profile of amino acids for protein synthesis." [*Id.* at § 1.]

21. The FDA-approved labeling for ELCYS® further instructs healthcare providers that "ELCYS is for *admixing use* only. It is *not for direct intravenous infusion*. Prior to administration, ELCYS *must be diluted and used as an admixture* in parenteral nutrition (PN) solutions. The resulting solution is for intravenous infusion into a central or peripheral vein." [*Id.* at § 2.1 (emphases in original).] It goes on to provide instructions for healthcare providers on how to prepare the admixture by following the steps laid out on the label and how to administer PN solutions containing ELCYS®. [*Id.* at §§ 2.2-2.5.]

22. The FDA-approved labeling for ELCYS® further instructs healthcare providers to "Remove ELCYS vial from the carton and inspect for particulate matter." [*Id.* at § 2.3.]

23. The FDA-approved labeling for ELCYS® further instructs healthcare providers to "Visually inspect the diluted PN solution containing ELCYS for particulate matter before admixing, after admixing, and prior to administration. The solution should be clear and there should be no precipitates." [*Id.* at § 2.2.]

24. The FDA-approved labeling for Exela's ELCYS® product provides recommended dosage and volume for pediatric patients from birth to less than 12 years of age, including for neonates and infants, e.g., preterm and term infants less than 1 month of age, and pediatric patients 1 month to less than 1 year of age. [*Id.* at § 2.5 & Tbl. 1.]

25. The FDA-approved labeling for ELCYS® instructs that "[t]he dosage of the final PN solution containing ELCYS must be based on the concentrations of all components in the solution and the recommended nutritional requirements *[see Dosage and Administration (2.5)]*." [*Id.* § 2.4.]

26. The FDA-approved labeling for ELCYS® includes the following warnings related to the level of aluminum patients receive: "Aluminum may reach toxic levels with prolonged parenteral administration in patients with renal impairment. Preterm infants are particularly at risk for aluminum toxicity because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which also contain aluminum. Patients with renal impairment, including preterm infants, who receive greater than 4 to 5 mcg/kg/day of parenteral aluminum can accumulate aluminum to levels associated with central nervous system and bone toxicity." [*Id.* at § 5.7.] It further instructs, "[e]xposure to aluminum from ELCYS is not more than 0.21 mcg/kg/day when preterm and term infants less than 1 month of age are administered the

recommended maximum dosage of ELCYS® (15 mg cysteine/g of amino acids and 4 g of amino acids/kg/day) *[see Table 1, Dosage and Administration (2.5)]*. When prescribing ELCYS for use in PN containing other small volume parenteral products, the total daily patient exposure to aluminum from the admixture should be considered and maintained at no more than 5 mcg/kg/day *[see Use in Specific Populations (8.4)]*." [*Id.*]

B. The Asserted '155 Patent

27. On March 10, 2020, the USPTO issued the '155 patent, entitled "Stable, Highly Pure L-Cysteine Compositions for Injection and Methods of Use," and naming John Maloney, Aruna Koganti, and Phanesh Koneru as inventors. A copy of the '155 patent is attached to this Complaint as Exhibit C. The '155 patent is listed in the Orange Book in association with Exela's ELCYS® product.

28. The '155 patent is assigned to Plaintiff Exela.

29. Claim 1 of the '155 patent reads as follows:

> A method of treating a subject having an adverse health condition that is responsive to L-cysteine administration, said method comprising:
> parenterally administering to said subject a parenteral composition comprising a mixture of one or more amino acids, intravenous fluid, and a stable L-cysteine composition, wherein said stable L-cysteine composition contributes to said parenteral composition:
> a therapeutically effective amount of L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof;
> per Liter of said stable L-cysteine composition, from about 1.0 mcg to about 250 mcg of Aluminum;
> not more than about 2.0 wt % of cystine relative to L-cysteine; and,
> not more than about 2.0 wt % of pyruvic acid relative to L-cysteine.

30. Claim 27 of the '155 patent reads as follows:

> A method of treating a subject having an adverse health condition that is responsive to L-cysteine administration, said method comprising:

parenterally administering to said subject a parenteral composition comprising a mixture comprising a stable L-cysteine composition, wherein said stable L-cysteine composition contributes to said parenteral composition:
a therapeutically effective amount of L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof;
per Liter of said stable L-cysteine composition, not more than about 150 mcg of Aluminum;
cystine relative to L-cysteine not more than about 2.0 wt%; and
pyruvic acid relative to L-cysteine not more than about 2.0 wt%.

31. Exela's ELCYS® product, and its use according to the directions and instructions on the FDA-approved label, is covered by at least claims 1 and 27 of the '155 patent.

32. Claim 27 of the '155 patent was previously found not invalid by this Court after a bench trial with substantial expert testimony. *Exela Pharma Scis., LLC v. Eton Pharms., Inc.*, __ F. Supp. 3d ___, 2022 WL 3278735 (D. Del. Aug. 8, 2022).

C. The Asserted '941 Patent

33. On November 29, 2022, the USPTO issued the '941 patent, entitled "Stable, Highly Pure L-Cysteine Compositions for Injection and Methods of Use," and naming John Maloney, Aruna Koganti, and Phanesh Koneru as inventors. A copy of the '941 patent is attached to this Complaint as Exhibit D. The '941 patent is listed in the Orange Book in association with Exela's ELCYS® product.

34. The '941 patent is assigned to Plaintiff Exela.

35. Claim 1 of the '941 patent reads as follows:

A solution of L-cysteine comprising,
L-cysteine or a pharmaceutically acceptable salt thereof and/or hydrate thereof in an amount from about 10 mg/mL to about 100 mg/mL;
not more than 200 ppb of aluminum for at least 6 months from the time of manufacture of the solution;
not more than 2.0% L-cystine relative to L-cysteine; and,
a pharmaceutically acceptable carrier; and,
wherein the solution:
has a pH from about 1.0 to about 2.5;
is substantially free of visually detectable particulate matter; and,

is suitable for use as an additive in a parenteral nutrition composition for administration to an individual.

36. Claim 6 of the '941 patent, which depends from claim 1, reads as follows:

The solution of claim 1, comprising not more than 150 ppb of aluminum for at least 12 months from the time of manufacture of the solution.

37. Exela's ELCYS® product is covered by at least claims 1 and 6 of the '941 patent.

DECLARATORY JUDGMENT JURISDICTION

38. On or about January 26, 2023, FDA approved Nivagen's ANDA No. 213073 for an injectable Generic Cysteine Hydrochloride product with a cysteine hydrochloride concentration of 7.25% ("Nivagen's Product"). [Exhibit E (FDA Table of Competitive Generic Therapeutics Approvals)] Nivagen is thus free to launch its Product at any time.

39. On information and belief, Nivagen's entry into the market is imminent as it has already begun contacting potential customers regarding offers for sale of its Product and proposing a significant discount to the list price of ELCYS®. Central Admixture Pharmacy Services Inc. ("CAPS") is the nation's largest network of outsourcing admixture pharmacies. CAPS is also Exela's top single end-use customer. On Tuesday, January 31, 2023, CAPS informed Exela's Chief Commercial Officer Mark Hartman that a Nivagen representative contacted CAPS about Nivagen's 7.25% cysteine hydrochloride injection product and indicated to CAPS that Nivagen would soon launch its Product at a price 30% below Exela (on a milligram per milligram of cysteine delivered basis compared to ELCYS®).

40. A commercial launch of Navigen's Product, including sales and offers for sale, would destroy the market for Exela's ELCYS® product and irreparably harm Plaintiff.

41. The facts alleged herein show that a substantial controversy exists between Exela and Nivagen, parties having adverse legal interests, regarding infringement of the '155 and '941

patents, and that this controversy is of sufficient immediacy and reality to warrant the issuance of a declaratory judgment.

INFRINGEMENT BY NIVAGEN

42. The RLD for Nivagen's ANDA No. 213073 is the Hospira Cysteine Hydrochloride Product. [*Id.*]

43. Nivagen's Product, as a generic drug based on NDA No. 19523 for the Hospira Cycsteine Hydrochloride Product, would be required to have the same active ingredient, route of administration, dosage form, and strength as the Hospira Cysteine Hydrochloride Product. In addition, the conditions of use of Nivagen's Product must be the same as the conditions of use for the Hospira Cycsteine Hydrochloride Product. Further, section 505(j)(2)(A)(v) of the Federal Food, Drug and Cosmetics Act ("FDCA") requires that ANDAs contain information to show that the labeling proposed for the new drug is the same as the labeling for the RLD (with limited exceptions). Thus, the "indication" for the Nivagen Product must be identical to the indication of the Hospira Cycsteine Hydrochloride Product, which is also identical to the indication of ELCYS®. Thus, on information and belief, Nivagen's labeling states that the Product is "indicated to meet the nutritional requirements of newborn infants requiring total parenteral nutrition (TPN); and of adult and pediatric patients with severe liver disease who may have impaired enzymatic processes and require TPN. It can also be added to amino acid solutions to provide a more complete profile of amino acids for protein synthesis." [Exhibit G (Hospira Label) at Section 1] This matches what the ELCYS® labeling states. [Exhibit B (ELCYS® Label) at Section 1).]

44. Cysteine hydrochloride products do not have other uses aside from treating patients having an adverse health condition responsive to L-cysteine. [Exhibit I (Kuhn 3/14/2022 Trial Testimony) at 117:5-8.]

45. Because the Hospira Cycsteine Hydrochloride Product is older and has been withdrawn from the market, FDA would have expected Nivagen to make labeling changes to reflect new regulatory requirements and advances in scientific knowledge. FDA Guidance on Updating ANDA Labeling After the Market Application for the Reference Listed Drug Has Been Withdrawn instructs that such labeling changes may be needed "to achieve consistency with the labeling of other products that have the same active ingredient or an active ingredient in the same pharmacological or therapeutic class, or with the labeling of other products approved for the same indication, where appropriate." [Exhibit F (7/2016 FDA Guidance) at 5.]

46. As such, on information and belief, Nivagen's Product will be sold and distributed with labeling that includes substantially the same information that appears on the label for the Hospira Cysteine Hydrochloride Product (the RLD for Nivagen's Product), as well as the updates to that information that appear on the label for ELCYS® (which also relies on Hospira as its RLD). [Exhibit G (Hospira Label).] Indeed, the approved NDA for the NOURESS cysteine hydrochloride product (a product that has never been marketed), also relied on the Hospira product as the RLD, and the NOURESS approved label includes substantially the same information from the Hospira label, with the updates that appear on the label for ELCYS®. [Exhibit H (Nouress label).]

47. For example, on information and belief, the labeling for Nivagen's Product, like the labeling for both the Hospira Cysteine Hydrochloride Product and ELCYS®, contains recommended dosage and volume for pediatric patients. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® Label) at §§ 2.4 and 2.5.] Based on that information, which appears in the dosage and administration section of the labels, Nivagen's Product will be

used to treat neonates and infants with a therapeutically effective amount of L-cysteine. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® Label) at §§ 2.4 and 2.5.]

48. Nivagen's Product contains L-cysteine hydrochloride monohydrate in an amount from 10-100 mg/mL. Specifically, Nivagen's Product contains 72.5 mg/mL of L-cysteine hydrochloride monohydrate. [Exhibit E (FDA CGT Chart).] Cysteine hydrochloride is a pharmaceutically acceptable salt of L-cysteine. [Exhibit I (Kuhn 3/14/2022 Trial Testimony) at 119:12-16.]

49. Like both the Hospira Cysteine Hydrochloride Product and ELCYS®, Nivagen's Product comprises water as the pharmaceutically acceptable carrier for L-cysteine. [Exhibit G (Hospira Label) at Description; Exhibit B (ELCYS® Label) at § 11.] Water for injection is the intravenous fluid used in TPN solutions to allow for proper mixing of the components, including cysteine hydrochloride and amino acids. [Exhibit I (Kuhn 3/14/2022 Trial Testimony) at 78:11-24.]

50. Nivagen's Product is suitable for use as an additive in a parenteral nutrition composition for intravenous administration to an individual, as evidenced at least by FDA's approval of ANDA No. 213073 and the Product's indication.

51. On information and belief, like both the Hospira Cysteine Hydrochloride Product and ELCYS®, Nivagen's Product has a pH range from about 1.0 to about 2.5. [Exhibit G (Hospira Label) at Description; Exhibit B (ELCYS® Label) at § 11.]

52. Nivagen's Product is stable, as evidenced at least by FDA's approval of ANDA No. 213073.

53. Nivagen's Product is substantially free of visually detectable particulate matter, as evidenced at least by FDA's approval of ANDA No. 213073. Particulates are dangerous in

injectable compositions and create a safety concern. [Exhibit C ('155 Patent) at 5:7-9.] Labels for parenteral drug products are required to state "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit." 21 C.F.R. 201.57(c)(3)(iv). This statement appears on both the Hospira and ELCYS® labels and, on information and belief, also appears in the labeling for Nivagen's Product.

54. On information and belief, Nivagen's Product contains no more than 500 mcg/L of aluminum. FDA Regulation 21 C.F.R. § 201.323 requires all small volume parenteral drugs ("SVPs") that contain aluminum, such as cysteine hydrochloride products, include an aluminum toxicity warning on their labels that sets a maximum daily aluminum exposure for neonates of 4 to 5 µg/kg/day. FDA has informed Exela and at least two other cysteine manufacturers that the daily limit for aluminum exposure from the SVP cysteine hydrochloride, specifically, would be set at 0.6 mcg/kg/day. In addition, on December 2022, FDA issued a Guidance titled *Small Volume Parenteral Drug Products and Pharmacy Bulk Packages for Parenteral Nutrition: Aluminum Content and Labeling Recommendations, a draft guidance for industry on how to derive the recommended aluminum concentration limit in a small volume parenteral drug product based on that maximum daily exposure*, in which FDA used its previously disclosed aluminum exposure limit of 0.6 mcg/kg/day to calculate the aluminum concentration limit for a 7.25% cysteine hydrochloride product. [Exhibit J (12/2022 Guidance) at § III.] According to FDA's calculation, the maximum allowable aluminum concentration for a 7.25% cysteine hydrochloride product is 500 mcg/L (or, 500 "parts per billion" or "ppb"). [*Id.* at § 2, Table 2.] Accordingly, on information and belief, Nivagen's Product contains no more than 500 mcg/L

aluminum, as FDA would not have approved Nivagen's Product if it exceeded that aluminum amount at any time throughout its shelf-life.

55. On information and belief, Nivagen's label includes the following statement, as required by 21 C.F.R. § 201.323(e): "WARNING: This product contains aluminum that may be toxic. . . . ." As such, on information and belief, Nivagen's Product contains aluminum.

56. By seeking and obtaining approval for its Product to contain no more than 500 mcg/L of aluminum, Nivagen has sought and obtained approval to market Products that contain aluminum in the amounts recited in Exela's patent claims identified above, through the Product's shelf-life. To the extent that Nivagen's Product label indicates a lower aluminum concentration limit than 500 mcg/L, Nivagen has sought and obtained approval to market Products that contain aluminum in the amounts recited in Exela's patent claims identified above, through the Product's shelf-life.

57. On information and belief, Nivagen's Product has a shelf life of at least twelve months. Cysteine hydrochloride products, including ELCYS® and at least two other cysteine products previously approved by FDA, generally have a shelf life of 24 months, and on information and belief, Nivagen's Product would also have a 24 month shelf life. As a result, Nivogen's Product will maintain an aluminum level at or below its labeled amount for at least six months and at least 12 months from the time of manufacture of the solution.

58. Cystine and pyruvic acid have both been observed as degradation products of L-cysteine. ICH Guidelines on Impurities in New Drug Products limit each degradation product to a maximum of 1.0% of the drug substance. [Exhibit K (ICH Q3B R2 at Attachment 1).] Consistent with these guidelines, FDA approved ELCYS® with a specification limiting total impurities to no more than 2.0%. On information and belief, FDA would not thereafter approve

another cysteine hydrochloride product that permitted total impurities at a level greater than 2.0%, and thus on information and belief, Nivagen's Product specification limits total impurities to 2.0% and Nivagen's Product thus contains no more than 2.0% of either cystine or pyruvic acid. Moreover, this Court has previously construed the limitation, found in claim 27 of the '155 patent, "not more than about 2.0 wt %," to include none of the recited component. [C.A. No. 20-365 (MN) D.I. 244 at 44-45.] Thus, by seeking and obtaining approval for Products containing than less 2.0% total impurities, Nivagen necessarily sought and obtained approval for Products containing cystine in the amounts recited in Exela's patent claims identified.

59. Similarly, by seeking and obtaining approval for Products containing less than 2.0% total impurities, Nivagen necessarily sought and obtained approval for Products containing pyruvic acid in the amounts recited in Exela's patent claims identified.

60. On information and belief, the labeling for Nivagen's Product, like the labels for both Hospira Cysteine Hydrochloride Product and ELCYS®, instructs healthcare providers that, prior to administration, the product must be diluted and used as an admixture in parenteral nutrition solutions. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® Label) at §§ 2.1, 2.2, 2.3.] Like the labels for the Hospira Cysteine Hydrochloride Product and ELCYS®, the label for Nivagen's Product must therefore provide instructions as to how to prepare that admixture for use in a TPN solution. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® Label) at §§ 2.2-2.3.]

61. On information and belief, the label for Nivagen's Product, like the labels for both the Hospira Cysteine Hydrochloride Product and ELCYS®, provides instructions for admixing the product with one or more amino acids to form a parenteral composition. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® Label) at §§ 2.1, 2.2, 2.3.]

62. The label for Nivagen's Product contains the aluminum toxicity warning required by 21 C.F.R. § 201, about patients receiving greater than 4 to 5 mcg/kg/day of parenteral aluminum. [Exhibit B (ELCYS® Label) at § 5.7.] On information and belief, following the instructions on the label for Nivagen's Product results in a parenteral nutrition regimen with aluminum present in an amount from 1-2 to 4-5 micrograms/kg/day.

63. On information and belief, the labeling for the Nivagen's Product, like the labels for both the Hospira Cysteine Hydrochloride Product and ELCYS®, instructs healthcare providers that the dosage of the final TPN solution must be based on the concentrations of amino acids in the TPN solution and the recommended nutritional requirements. [Exhibit G (Hospira Label) at Dosage and Administration; Exhibit B (ELCYS® label) at § 2.4] The dose of cysteine hydrochloride administered is based on the individual patient's nutritional needs. [Exhibit I (Kuhn 3/14/2022 Trial Testimony at 119:20-120:3)] For example, the ELCYS® label instructs healthcare providers to use a dose of 15 mg cysteine base (22 mg cysteine hydrochloride) for each gram of amino acid administered to pediatric patients under 11 years of age. [Exhibit B (ELCYS® label) at § 2.5] FDA's guidance on aluminum also assumes that same clinical dosage of 15 mg cysteine base per gram of amino acid and a clinical dose of 4 grams/kg/day in its calculation of the aluminum concentration limit for cysteine hydrochloride. [Exhibit J (12/2022 Guidance) at § IV.B, Table 2.] On information and belief, and given FDA's approval of Nivagen's ANDA, when used as directed on the label Nivagen's Product will be dosed in the same or similar manner to provide a therapeutically effective amount of L-cysteine to patients. [*Id.* at §§ 1, 2.4, 2.5.]

64. For the reasons above, Nivagen has obtained approval to commercially market and sell cysteine solutions that meet all the limitations of at least claims 1 and 6 of the '941

patent, either literally or under the doctrine of equivalents; therefore, the product Nivagen offers to sell and sells will infringe Exela's '941 patent.

65. On information and belief, healthcare providers will admix Nivagen's Product according to the instructions on Nivagen's label and parenterally administer those compositions to patients who require TPN.

66. On information and belief, when healthcare providers admix Nivagen's Product according to the instructions on Nivagen's label to prepare compositions for a TPN regimen and/or administer those compositions to patients who require TPN, they will satisfy all the limitations of at least claims 1 and 27 of the '155 patent, either literally or under the doctrine of equivalents.

67. Accordingly, on information and belief, healthcare providers that follow the instructions on the labeling for Nivagen's Product will directly infringe at least some claims of the'155 patent.

COUNT I

(Infringement of the '155 Patent Under 35 U.S.C. § 271(b) & (c))

68. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

69. On information and belief, Nivagen monitors the status of patent applications filed by Exela that relate to L-cysteine drug products and the contents of the Orange Book for the RLDs related to cysteine hydrochloride products and/or serving as the basis for its ANDA submissions, including ELCYS®.

70. On information and belief, Nivagen became aware of the '155 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering methods of using ELCYS®. On information and belief, Nivagen has followed the *Exela Pharma Sciences,*

LLC v. Eton Pharmaceuticals, Inc. litigation and is therefore aware of the '155 patent. Thus, on information and belief, Nivagen has actual knowledge of the '155 patent.

71. On information and belief, Nivagen engages in the commercial manufacture, use, offer for sale, sale, importation or other promotion and/or distribution of Nivagen's Product.

72. On information and belief, Nivagen includes within the packaging of its Product, or otherwise makes available to healthcare providers and patients, labeling that instructs healthcare providers to perform the method of at least claims 1 and 27 of the '155 patent.

73. On information and belief, healthcare providers administering a parenteral nutrition regimen including Nivagen's Product within the United States according to the instructions in the product's labeling will directly infringe at least claims 1 and 27 of the '155 patent, either literally or under the doctrine of equivalents.

74. On information and belief, Nivagen possesses specific intent to encourage direct infringement of at least claims 1 and 27 of the '155 patent, including because Nivagen's labeling for its Product instructs users to perform the patented methods, providing evidence of an affirmative intent to induce infringement. Furthermore, because Nivagen's Product has no substantial non-infringing uses, Nivagen intends for the administration of its Product to directly infringe at least claims 1 and 27 of the '155 patent.

75. On information and belief, upon awareness of the '155 patent, Nivagen either actually knew of the potential for infringement of at least claims 1 and 27 of the '155 patent, or was willfully blind as to the potential for that infringement at least because Nivagen provides instructions for infringement of at least claims 1and 27 of the '155 patent in its labeling.

76. The commercial making, using, offering to sell, importing, or otherwise promoting and/or distributing of Nivagen's Product, with its labeling, constitutes an act of active inducement of infringement of at least claims 1 and 27 of the '155 patent.

77. On information and belief, Nivagen knows that its Product is a material part of the method of at least claims 1 and 27 of the '155 patent, including as evidenced in the contents of its label. On information and belief, Nivagen's Product was especially made or especially adapted for use by a healthcare provider in a manner that will directly infringe at least claims 1 and 27 of the '155 patent, as evidenced by the contents of its labeling. On information and belief, Nivagen's Product is not a staple article of commerce suitable for substantial non-infringing use, as evidenced by the contents of its labeling and the fact that it has obtained FDA approval for a particular use. There are no suitable uses for cysteine hydrochloride injections other than treating patients pursuant to FDA's approval for such products.

78. Thus, on information and belief, Nivagen contributes to the infringement of the claims of the '155 patent in this District and elsewhere in the United States by offering to sell, selling, importing, or otherwise distributing Nivagen's Product, which is a material for use in practicing the method of at least claims 1 and 27 of the '155 patent.

79. The commercial making, using, offering to sell, importing, or otherwise promoting and/or distributing of Nivagen's Product in violation of Plaintiff's patent rights will cause harm to Plaintiff, for which damages are inadequate.

80. Unless and until Nivagen is enjoined from infringing the '155 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

81. Despite Defendant's knowledge of and notice of the '155 patent and its ongoing infringement, Defendant continues to manufacture, use, sell, offer for sale, and/or import its

Product in a manner that infringes the '155 Patent. Defendant lacks a justifiable belief that it does not infringe the '155 patent, or that the '155 patent is invalid, and has acted recklessly in its infringing activity, justifying an increase in the damages to be awarded Plaintiff up to three times the amount found or assessed, in accordance with 35 U.S.C. § 284.

82. At least Defendant's willful infringement of the '155 patent renders this case an exceptional case, justifying an award to Plaintiff of its reasonable attorneys' fees, in accordance with 35 U.S.C. § 285.

COUNT II

(Declaratory Judgment of Infringement of the '155 Patent Under 35 U.S.C. § 271(b) & (c))

83. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

84. This claim arises under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

85. There is an actual case or controversy such that the Court may entertain Plaintiff's request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

86. On information and belief, Nivagen monitors the status of patent applications filed by Exela that relate to L-cysteine drug products and the contents of the Orange Book for the RLDs related to cysteine hydrochloride products and/or serving as the basis for its ANDA submissions, including ELCYS®.

87. On information and belief, Nivagen became aware of the '155 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering methods of using ELCYS®. On information and belief, Nivagen has followed the *Exela Pharma Sciences, LLC v. Eton Pharmaceuticals, Inc*. litigation and is therefore aware of the '155 patent.

88. On information and belief, Nivagen will engage in the commercial offer for sale, sale, importation and/or other distribution of Nivagen's Product immediately and imminently given FDA approval of ANDA No. 213073 and that Nivagen has already reached out to customers about the potential launch of its product and suggested that it would come on the market at a price 30% lower than Exela's price for ELCYS®.

89. Nivagen's actions, including but not limited to the development of Nivagen's Product, the filing and approval of an ANDA, and that Nivagen has already reached out to customers about the potential launch of its product and suggested that it would come on the market at a price 30% lower than Exela's price for ELCYS®, reliably predict that Nivagen has made and will continue to make substantial preparation in the United States, including in the District of Delaware, to sell, offer to sell, import and/or otherwise distribute its Product.

90. On information and belief, Nivagen includes within the packaging of its Product, or otherwise makes available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claims 1 and 27 of the '155 patent.

91. On information and belief, healthcare providers administering a parenteral nutrition regimen including Nivagen's Product within the United States according to the instructions in the product's labeling will directly infringe at least claims 1 and 27 of the '155 patent, either literally or under the doctrine of equivalents.

92. On information and belief, Nivagen possesses specific intent to encourage direct infringement of at least claims 1 and 27 of the '155 patent, including because Nivagen's labeling for its Product instructs users to perform the patented methods, providing evidence of an affirmative intent to induce infringement. Furthermore, because Nivagen's Product has no

substantial non-infringing uses, Nivagen intends for the administration of its Product to directly infringe at least claims 1and 27 of the ’155 patent.

93. On information and belief, upon awareness of the ’155 patent, Nivagen either actually knew of the potential for infringement of at least claims 1and 27 of the ’155 patent, or was willfully blind as to the potential for that infringement at least because Nivagen provides instructions for infringement of at least claims 1 and 27 of the ’155 patent in its labeling.

94. The commercial making, using, offering to sell, importing, or otherwise promoting and/or distributing of Nivagen’s Product, with its labeling, constitutes an act of active inducement of infringement of at least claims 1 and 27 of the ’155 patent.

95. On information and belief, Nivagen knows that its Product is a material part of the method of at least claims 1 and 27 of the ’155 patent, including as evidenced in the contents of its label. On information and belief, Nivagen’s Product was especially made or especially adapted for use by a healthcare provider in a manner that will directly infringe at least claims 1 and 27 of the ’155 patent, as evidenced by the contents of its labeling. On information and belief, Nivagen’s Product is not a staple article of commerce suitable for substantial non-infringing use, as evidenced by the contents of its labeling and the fact that it seeks FDA approval for a particular use. There are no suitable uses for cysteine hydrochloride injections other than treating patients pursuant to FDA’s approval for such products.

96. Thus, on information and belief, Nivagen will contribute to the infringement of the claims of the ’155 patent in this District and elsewhere in the United States by offering to sell, selling, importing, or otherwise distributing Nivagen’s Product, which is a material for use in practicing the method of at least claims 1 and 27 of the ’155 patent.

97. The commercial offering to sell, selling, importing and/or other distribution of Nivagen's Product for use in practicing the patented methods in violation of Plaintiff's patent rights will cause harm to Plaintiff, for which damages are inadequate.

98. Plaintiff is entitled to a declaratory judgment that the future offer for sale, sale, importation and/or other distribution of Nivagen's Product before patent expiration will constitute contributory infringement of at least claims 1 and 27 of the '155 patent under 35 U.S.C. § 271(c).

99. Unless and until Nivagen is enjoined from infringing the '155 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

COUNT III

(Infringement of the '155 Patent Under 35 U.S.C. § 271(e)(2))

100. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

101. Nivagen submitted ANDA No. 213073 to the FDA under section 505(j) of the FDCA to obtain approval to engage in the commercial manufacture, importation, use, sale, or offer for sale of Nivagen's Product throughout the United States. The subject of Nivagen's ANDA—Nivagen's Product—is a drug the use of which (as evidenced by its labeling) is claimed in the '155 patent. By submitting ANDA No. 213073 to FDA, Nivagen has committed an act of infringement of the '155 patent under 35 U.S.C. § 271(e)(2)(A).

102. The use of Nivagen's Product according to the instructions in the product's label will constitute an act of direct infringement of the '155 patent, either literally or under the doctrine of equivalents.

103. On information and belief, Nivagen monitors the status of patent applications filed by Exela that relate to L-Cysteine drug products and the contents of the Orange Book for the RLDs serving as the basis for its ANDA submissions, including ELCYS®.

104. On information and belief, Nivagen became aware of the '155 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering methods of using ELCYS®. On information and belief, Nivagen has followed the *Exela Pharma Sciences, LLC v. Eton Pharmaceuticals, Inc*. litigation and is therefore aware of the '155 patent.

105. On information and belief, Nivagen knew or should have known that its commercial making, offering to sell, selling, importing, or otherwise promoting and/or distributing of Nivagen's Product, with its labeling, will actively induce the direct infringement of the '155 patent.

106. On information and belief, Nivagen knew or should have known that Nivagen's Product will be especially made or especially adapted for use in an infringement of the '155 patent, and is not a staple article or commodity of commerce suitable for substantial non-infringing use, as evidenced by, for example, the contents of its labeling. And, on information and belief, Nivagen knew or should have known that its commercial offering to sell, selling, importing or otherwise distributing of Nivagen's Product with its labeling will actively contribute to the direct infringement of the '155 patent.

107. Unless and until Nivagen is enjoined from infringing the '155 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

108. Plaintiff is entitled to the relief provided by 35 U.S.C. § 271(e)(4), including an order of this Court stating that the effective date of final approval of Nivagen's ANDA No. 213073 be a date that is not earlier than the expiration date of the '155 patent.

COUNT IV

(Infringement of the '941 Patent Under 35 U.S.C. § 271(a))

109. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

110. On information and belief, Nivagen monitors the status of patent applications filed by Exela that relate to L-cysteine drug products and the contents of the Orange Book for the RLDs related to cysteine hydrochloride products and/or serving as the basis for its ANDA submissions, including ELCYS®.

111. On information and belief, Nivagen became aware of the '941 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering ELCYS®. Thus, on information and belief, Nivagen has actual knowledge of the '941 patent.

112. On information and belief, Nivagen engages in the commercial manufacture, use, offer for sale, sale, and/or importation of Nivagen's Product.

113. On information and belief, Nivagen's Product practices all limitations of at least claims 1 and 6 of the '941 patent, either literally or under the doctrine of equivalents, as detailed above, and thus the manufacture, importation, use, sale, and/or offer for sale of Nivagen's Product will constitute an act of infringement of the '941 patent.

114. The commercial manufacture, importation, use, sale, or offer for sale of Nivagen's Product in violation of Plaintiff's patent rights will cause harm to Plaintiff, for which damages are inadequate.

115. Unless and until Nivagen is enjoined from infringing the '941 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

116. Despite Defendant's knowledge of and notice of the '941 patent and its ongoing infringement, Defendant continues to manufacture, use, sell, offer for sale, and/or import its Product in a manner that infringes the '941 Patent. Defendant lacks a justifiable belief that it does not infringe the '941 patent, or that the '941 patent is invalid, and has acted recklessly in its

infringing activity, justifying an increase in the damages to be awarded Plaintiff up to three times the amount found or assessed, in accordance with 35 U.S.C. § 284.

117. At least Defendant's willful infringement of the '941 patent renders this case an exceptional case, justifying an award to Plaintiff of its reasonable attorneys' fees, in accordance with 35 U.S.C. § 285

COUNT V

(Declaratory Judgment of Infringement of the '941 Patent Under 35 U.S.C. § 271(a))

118. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

119. This claim arises under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

120. There is an actual case or controversy such that the Court may entertain Plaintiff's request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

121. On information and belief, Nivagen monitors the status of patent applications filed by Exela that relate to L-cysteine drug products and the contents of the Orange Book for the RLDs related to cysteine hydrochloride products and/or serving as the basis for its ANDA submissions, including ELCYS®.

122. On information and belief, Nivagen became aware of the '941 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering ELCYS®. Thus, on information and belief, Nivagen has actual knowledge of the '941 patent.

123. On information and belief, Nivagen will engage in the commercial manufacture, use, offer for sale, sale, and/or importation of Nivagen's Product immediately and imminently given FDA approval of ANDA No. 213073 and that Nivagen has already reached out to

customers about the potential launch of its product and suggested that it would come on the market at a price 30% lower than Exela's price for ELCYS®.

124. Nivagen's actions, including but not limited to the development of Nivagen's Product, the filing and approval of an ANDA, and that Nivagen has already reached out to customers about the potential launch of its product and suggested that it would come on the market at a price 30% lower than Exela's price for ELCYS®, reliably predict that Nivagen has made and will continue to make substantial preparation in the United States, including in the District of Delaware, to manufacture, sell, offer to sell, and/or import Nivagen's Product.

125. On information and belief, Nivagen's Product practices all limitations of at least claims 1 and 6 of the '941 patent, either literally or under the doctrine of equivalents, as detailed above, and thus the manufacture, importation, use, sale, and/or offer for sale of Nivagen's Product will constitute an act of infringement of the '941 patent.

126. The commercial manufacture, importation, use, sale, or offer for sale of Nivagen's Product in violation of Plaintiff's patent rights will cause harm to Plaintiff, for which damages are inadequate.

127. Plaintiff is entitled to a declaratory judgment that the future manufacture, use, offer for sale, sale and/or importation of Nivagen's Product before patent expiration will constitute direct infringement of at least claims 1 and 6 of the '941 patent under 35 U.S.C. § 271(a).

128. Unless and until Nivagen is enjoined from infringing the '941 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

COUNT VI

(Infringement of the '941 Patent Under 35 U.S.C. § 271(e)(2))

129. Plaintiff incorporates each of the preceding paragraphs as if fully set forth herein.

130. Nivagen submitted ANDA No. 213073 to the FDA under section 505(j) of the FDCA to obtain approval to engage in the commercial manufacture, importation, use, sale, or offer for sale of Nivagen's Product throughout the United States. The subject of Nivagen's ANDA—Nivagen's Product—is a drug claimed in the '941 patent. By submitting ANDA No. 213073 to FDA, Nivagen has committed an act of infringement of the '941 patent under 35 U.S.C. § 271(e)(2)(A).

131. The commercial manufacture, importation, use, sale, or offer for sale of Nivagen's Product will constitute an act of direct infringement of the '941 patent, either literally or under the doctrine of equivalents.

132. Unless and until Nivagen is enjoined from infringing the '491 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

133. Plaintiff is entitled to the relief provided by 35 U.S.C. § 271(e)(4), including an order of this Court stating that the effective date of final approval of Nivagen's ANDA No. 213073 be a date that is not earlier than the expiration date of the '941 patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff prays for the following relief:

A. That a finding be made that Nivagen has infringed one or more claims of the '155 Patent;

B. That a finding be made that Nivagen has infringed one or more claims of the '941 Patent;

C. That a finding be made that Nivagen's infringement of the '155 and '941 Patents has been and is willful;

D. That an order be issued preliminarily and permanently enjoining Nivagen and its affiliates, subsidiaries, officers, agents, employees, attorneys, and all persons in active concert or participation with any of them, or acting on their behalf, from infringing the '155 and '941 patents;

E. That an award be granted to Exela of damages adequate to compensate Exela for all infringement occurring through the date of judgment, including Exela's lost profits, with prejudgment interest, and for any supplemental damages as appropriate and post-judgment interest after that date;

F. That judgment be issued that Nivagen has infringed the '155 and '941 patents under 35 U.S.C. § 271(e)(2)(A) by submitting ANDA 213073 under section 505(j) of the Federal Food, Drug and Cosmetic Act, and that the commercial manufacture, use, offer to sell, or sale within the United States, or importation into the United States, of Nivagen's Product constitutes an act of infringement of the '155 and '941 patents;

G. That an order be issued under 35 U.S.C. § 271(e)(4)(A) that the effective date of FDA approval of Nivagen's ANDA No. 213073 shall be a date which is not earlier than the expiration dates of the '155 and '941 patents, as extended by any applicable period of exclusivity;

H. That an injunction be issued under 35 U.S.C. § 271(e)(4)(B) permanently enjoining Nivagen, its officers, agents, servants, employees, licensees, representatives, and attorneys, and all other persons acting or attempting to act in active concert or participation with them or acting on their behalf, from engaging in the commercial manufacture, use, offer to sell, or sale within the United States, or importation into the United States, of any drug product covered by, or drug product whose use is covered by the '155 and '941 patents;

I. That a declaration be issued under 28 U.S.C. § 2201 that the manufacture, use, offer for sale, sale, and/or importation of Nivagen's Product before expiration of the'155 and '941 patents does and will infringe the'155 and '941 patents;

J. If Nivagen engages in the commercial manufacture, use, offer to sell, sale, or importation of Nivagen's Product prior to the expiration of the'155 and '941 Patents, as extended by any applicable period of exclusivity, judgment awarding Exela damages resulting from such infringement under 35 U.S.C. § 271(e)(4)(C), increased to treble the amount found and/or assessed together with prejudgment and post-judgment interest and costs under 35 U.S.C. § 284;

K. That an award be granted to Exela of enhanced damages under 35 U.S.C. § 284;

L. That this case be declared an exceptional case under 35 U.S.C. § 285, and that Exela be awarded reasonable attorneys' fees and costs;

M. That an accounting be performed of Nivagen's infringing activities not presented at trial and an award by the Court of additional damages for any such infringing sales; and

N. That this Court award such other and further relief as it may deem just and proper.

JURY TRIAL DEMANDED

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiff hereby demands a trial by jury of all issues so triable.

Dated: February 6, 2023

FISH & RICHARDSON P.C.

By: */s/ Douglas E. McCann*

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