

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

EXELA PHARMA SCIENCES, LLC,

Plaintiff,

v.

SANDOZ, INC.,

Defendant.

Civil Action No.: 1:20-cv-645-MN

**JURY TRIAL DEMANDED**

  
PUBLIC VERSION

**AMENDED COMPLAINT**

Plaintiff Exela Pharma Sciences, LLC (“Plaintiff” or “Exela”) by its attorneys, hereby alleges as follows in this amended complaint:

**NATURE OF ACTION**

1. This is an action for infringement of U.S. Patent No. 10,478,453 (“the ’453 patent”) and U.S. Patent No. 10,583,155 (“the ’155 patent”) under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.*, including §§ 271(e)(2), 271(a)-(c), and for a declaratory judgment of infringement of the ’453 and ’155 patents under 28 U.S.C. §§ 2201 and 2202 and 35 U.S.C. §§ 271(a)-(c). Plaintiff institutes this action to enforce its patent rights covering its FDA-approved ELCYS® brand L-cysteine hydrochloride injection.

**THE PARTIES**

2. Exela 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 Sandoz, Inc. (“Sandoz”) is a corporation organized and existing under the laws of the State of Colorado and having a principal place of business at 100 College Road West, Princeton, New Jersey 08540.

### **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 Sandoz because, on information and belief, Sandoz has purposely availed itself of the benefits and protections of the State of Delaware's laws such that it should reasonably anticipate being haled into court in this judicial district, and because this action arises from activities of Sandoz directed toward the State of Delaware.

6. On information and belief, Sandoz has engaged in systematic and continuous business contacts within the State of Delaware, regularly conducts business in the State of Delaware, and has purposefully availed itself of the privilege of doing business in the State of Delaware.

7. On information and belief, Sandoz develops, manufactures, imports, markets, offers to sell, and/or sells pharmaceutical drug products, including generic drugs, throughout the United States, including in the State of Delaware.

8. On information and belief, Sandoz derives substantial revenue from pharmaceutical drug products, including generic drugs, that are used and/or consumed within the State of Delaware, and which are manufactured by or for Sandoz and for which Sandoz is the named applicant on approved Abbreviated New Drug Applications ("ANDAs").

9. On information and belief, Sandoz contracts with drug wholesalers and distributors to supply pharmaceutical drug products, including generic drugs, for which Sandoz is the named applicant on approved ANDAs, throughout the United States, including in the State of Delaware.

10. On information and belief, the drug wholesalers and distributors Sandoz contracts with to supply pharmaceutical drug products, including generic drugs, are licensed to sell those products in the State of Delaware and are registered with the Delaware Board of Pharmacy as licensed “Pharmacy-Wholesale” and “Distributor/Manufacturer CSR.”

11. On information and belief, various products for which Sandoz is the named applicant on approved ANDAs are offered for sale to pharmacies and hospitals in the State of Delaware, distributed to and available at pharmacies and hospitals in the State of Delaware, prescribed by healthcare providers practicing in the State of Delaware, used by healthcare providers, patients, and/or hospitals in the State of Delaware, and/or administered to patients in the State of Delaware.

12. Sandoz has filed ANDA No. 209994 (“Sandoz’s ANDA”) for Cysteine Hydrochloride Injection, USP, 500 mg/10 mL (50 mg/mL) single-dose vials (“Sandoz’s ANDA Product”), which is a generic version of Exela’s ELCYS<sup>®</sup> product, containing paragraph IV certifications to Exela’s ’453 and ’155 patents.

13. Sandoz, through its counsel Abigail Langsam of the law firm Arnold & Porter Kaye Scholer LLP, sent a letter dated April 2, 2020 to Exela, a Delaware corporation, notifying Exela that Sandoz had filed with FDA, and FDA had received, Sandoz’s ANDA No. 209994 (“Sandoz’s Paragraph IV Letter”).

14. Sandoz’s filing of ANDA No. 209994 constitutes a formal act that reliably indicates Sandoz’s plans to engage in marketing of Sandoz’s ANDA Product throughout the United States, including in the State of Delaware, so that Sandoz’s ANDA Product will be used throughout the United States, including in the State of Delaware.

15. On information and belief, upon approval of ANDA No. 209994, Sandoz will engage in the marketing of the Sandoz ANDA Product and offer to sell and/or sell its ANDA Product either directly or indirectly through its established channels of distribution via one or more of its drug wholesalers and distributors throughout the United States, including in the State of Delaware.

16. On information and belief, Sandoz knows, expects, and intends that upon approval of ANDA No. 209994, Sandoz's ANDA Product will be offered for sale to hospitals and/or pharmacies in the State of Delaware, distributed to and available at hospitals and/or pharmacies in the State of Delaware, prescribed by healthcare providers practicing in the State of Delaware, used by healthcare providers, patients, and/or hospitals in the State of Delaware, and/or administered to patients in the State of Delaware.

17. Sandoz's marketing, offer to sell, and/or sales of its ANDA Product, and the use of its ANDA Product, throughout the United States, including in the State of Delaware, before expiry of Exela's '453 and '155 patents will constitute infringement of the '453 and '155 patents, resulting in harm and injury to Exela.

18. Further, this Court has personal jurisdiction over Sandoz because Sandoz regularly engages in patent litigation in this judicial district, has previously consented to personal jurisdiction and venue in such litigation in this judicial district, has purposefully availed itself of the rights and benefits of this Court numerous times by asserting claims and/or counterclaims in this Court, and has in the past consented and continues to consent to personal jurisdiction and venue in this judicial district. *See, e.g., Otsuka Pharmaceutical Co., Ltd. et al. v. Sandoz Inc. et al.*, 19-cv-02080, D.I. 11 (D. Del. March 16, 2020); *Merck Sharp & Dohme Corp. v. Sandoz Inc.*, 19-cv-00312, D.I. 10 (D. Del. April 10, 2019); *Astellas US LLC et al. v. Sandoz Inc.*, 18-cv-

01676, D.I. 13 (D. Del. Nov. 30, 2018); *Pharmacyclics LLC et al v. Sun Pharma Global FZE et al.*, 18-cv-00192, D.I. 12 (D. Del. Feb. 26, 2018); *H. Lundbeck A/S et al. v. Sandoz Inc. et al.*, 18-cv-00177, D.I. 9 (D. Del. April 13, 2018); *ViiV Healthcare Company et al. v. Sandoz Inc. et al.*, 17-cv-01784, D.I. 12 (D. Del. Jan. 24, 2018); *Biogen International GMBH et al. v. Sandoz Inc.*, 17-00874, D.I. 9 (D. Del. Oct. 16, 2017); *Bristol-Myers Squibb Company et al. v. Sandoz Inc.*, 17-cv-00407, D.I. 9 (D. Del. June 12, 2017); *Omeros Corporation v. Sandoz Inc.*, 17-cv-00799, D.I. 11 (D. Del. Sept. 13, 2017).

19. Venue is proper in this judicial district under at least 28 U.S.C. § 1391 and including because Sandoz is subject to personal jurisdiction in this judicial district, has previously consented to venue in this judicial district, and on information and belief will consent to venue in this judicial district for the purpose of this case.

20. Exela believes this case belongs in Delaware, but is also filing a case in the United States District Court for the District of Colorado out of an abundance of caution.

### **FACTUAL BACKGROUND**

#### **A. The Development and FDA Approval of Exela's ELCYS<sup>®</sup> L-Cysteine Hydrochloride Injection Product**

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

22. 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).

23. 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, including an unapproved product sold by Sandoz under FDA's drug "shortage" program, which purports to permit importation of unapproved drugs during a shortage (or in this case, absence) of an FDA-approved version of the drug in the United States. One significant drawback of such L-cysteine products is that they were known to contain high amounts of aluminum, labeled as containing up to as much as 5,000 micrograms/liter ("mcg/L," "µg/L" or, more commonly, "parts per billion" or "ppb").

24. 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.

25. FDA has long been concerned about the presence of aluminum in parenteral drug products.

26. As early as 1986, FDA held meetings to discuss the risks posed by aluminum in human drug products, including in parenteral drug products. Parenteral Drug Products Containing Aluminum as an Ingredient or a Contaminant; Notice of Intent and Request for Information, 55 Fed. Reg. 20799 (May 21, 1990).

27. In 1990, FDA gave public notice that it was considering proposing rules related to the aluminum content in parenteral drug products. *Id.* In particular, FDA stated it "has become

increasingly concerned about aluminum content in parenteral drug products, including aluminum present as a contaminant” because the literature contained reports “that neonates and other patient populations may be at high risk of exposure to unsafe amounts of aluminum in drug products.” *Id.* at 20800. FDA noted that “many drug products that are used routinely in parenteral therapy have been reported to contain levels of aluminum sufficiently high to cause clinical manifestations.” *Id.* FDA also expressed concern “that certain populations of patients may be exposed to excess aluminum parenterally,” including “premature neonates and neonates who have immature or impaired renal function [that] require total parenteral nutrition,” and patients with renal failure or comprised renal function. *Id.* FDA’s notice cites several articles reporting on the effects of aluminum in these susceptible patient populations. *Id.*

28. In 1998, and after a period of public comment, FDA proposed amending its regulations “to add certain labeling requirements concerning aluminum in large volume parenterals (LVP’s) and small volume parenterals (SVP’s) used in total parenteral nutrition (TPN).” Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition, 63 Fed. Reg. 176, 176 (Jan. 5, 1998). FDA proposed the regulations “because of evidence linking the use of parenteral drug products containing aluminum to morbidity and mortality among patients on TPN therapy, especially premature infants and patients with impaired kidney function.” *Id.*

29. L-cysteine hydrochloride injection is a Small Volume Parenteral (SVP) drug product used in TPN.

30. The regulation proposed in 1998 contained five parts: “(1) Establish a maximum permissible level of aluminum in LVP’s used in TPN therapy; (2) require that the maximum level of aluminum permitted in LVP’s used in TPN therapy be stated on the package insert of all

LVP's used in TPN therapy; (3) require that the maximum level of aluminum at expiry be stated on the immediate container label of SVP's and pharmacy bulk packages used in the preparation of TPN solutions; (4) require that the package insert of all LVP's and SVP's, including pharmacy bulk packages, contain a warning statement about aluminum toxicity in patients with impaired kidneys and neonates receiving TPN therapy; and (5) require that applicants and manufacturers develop validated assay methods for determining the aluminum content in parenteral drug products and that applicants submit the validated assay methods to FDA for approval." *Id.* at 177.

31. In 2000, FDA issued a regulation, 21 C.F.R. § 201.323, concerning aluminum in large and small volume parenterals used in total parenteral nutrition that would become effective January 26, 2001. Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition, 65 Fed. Reg. 4103 (Jan. 26, 2000). The regulation would, among other things, limit the aluminum content in all LVP's to 25 micrograms per liter (i.e., 25 parts per billion, or 25 ppb), require the container label for SVP's to state the maximum level of aluminum at expiry, require LVP and SVP package inserts to include a particular warning statement about aluminum toxicity, and require applicants for LVP and SVP products to use validated assay methods to determine aluminum content in the products and submit to FDA release data concerning aluminum content for several batches. *Id.* at 4104-4105.

32. In January 2001, FDA delayed the effective date of the regulation until January 26, 2003 based on feedback from the industry that more time was need to comply with it. Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition; Delay of Effective Date, 66 Fed. Reg. 7864 (Jan. 26, 2001).

33. In August 2002, FDA proposed amending the regulation to require container labeling for LVP's and SVP's containing 25 micrograms per liter ( $\mu\text{g/L}$ ) or less of aluminum to state "Contains no more than 25  $\mu\text{g/L}$  of aluminum" instead of the exact amount of aluminum they contain. Amendment of Regulations on Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition, 67 Fed. Reg. 52429 (Aug. 12, 2002).

34. In November 2002, FDA further delayed the effective date of the final regulation until January 26, 2004 to allow FDA time to finalize the amendment proposed in August 2002. Aluminum in Large and Small Volume Parenterals Used in Total Parenteral Nutrition; Amendment; Delay of Effective Date, 67 Fed. Reg. 70691 (Nov. 26, 2002).

35. In June 2003, FDA finalized the amendment to the regulation first proposed in August 2002. 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).

36. The regulation became effective on July 26, 2004, and is codified at 21 C.F.R. § 201.323. 68 Fed. Reg. 32,979 (June 3, 2003).

37. 21 C.F.R. § 201.323 requires that "the maximum level of aluminum present at expiry must be stated on the immediate container label of all small volume parenteral (SVP) drug products" unless the maximum level of aluminum is 25 mcg/L or less, in which case the immediate container label may state "Contains no more than 25 [micro]g/L of aluminum." 21 C.F.R. § 201.323(c)-(d).

38. 21 C.F.R. § 201.323(e) requires manufacturers of LVP's and SVP's to include the following warning on their product labeling:

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of

calcium and phosphate solutions, which contain aluminum. 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. Tissue loading may occur at even lower rates of administration.

21 C.F.R. § 201.323(e).

39. On information and belief, the safety concerns with and risks posed by aluminum exposure that drove FDA to enact 21 C.F.R. § 201.323 remain valid concerns today.

40. In May 2017, Exela submitted to FDA a New Drug Application (“NDA”) under Section 505(b) of the Federal Food, Drug, and Cosmetic Act seeking approval for an L-cysteine hydrochloride injection product, which is an SVP subject to 21 C.F.R. § 201.323. After 6 months of storage at 25 °C and 60% relative humidity, Exela’s L-cysteine hydrochloride product contained less than 570 mcg/L of aluminum. After 6 months of storage at 40 °C and 75% relative humidity, Exela’s L-cysteine hydrochloride product contained less than 1400 mcg/L of aluminum.

41. On August 4, 2017, FDA sent Exela a General Advice letter concerning Exela’s NDA signed on behalf of FDA by Dr. Donna Griebel, who at the time was the Director of the Division of Gastroenterology and Inborn Errors Products at FDA’s Center for Drug Evaluation and Research. [Ex. A (FDA’s August 4, 2017 letter to Exela).]

42. In the August 4, 2017 letter, FDA set forth a maximum aluminum content for 0.5g/10mL (50 mg/mL) L-cysteine hydrochloride injection products of no more than 145 mcg/L of aluminum during the product’s shelf life. [Ex. A at 1 (“a limit of  $\leq$  145 mcg/L aluminum is needed”).]

43. On information and belief, FDA’s August 4, 2017 letter to Exela sets forth FDA’s interpretation of 21 C.F.R. § 201.323, as applied specifically to L-cysteine hydrochloride

injection products (50 mg/mL), that the maximum amount of aluminum permitted in FDA approvable L-cysteine hydrochloride injection products (50 mg/mL) is no more than 145 mcg/L.

44. On information and belief, the scientific rationale underlying FDA's setting an aluminum limit for L-cysteine hydrochloride injection products (50 mg/mL) to no more than 145 mcg/L during the product's shelf life remains very much applicable today.

45. In April of 2019, after extensive effort, research, and development, including substantial work to achieve the  $\leq 145$  mcg/L aluminum level FDA mandated for the L-cysteine hydrochloride injection product, 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 that could be safely administered to newborn patients, including premature babies weighing as little as 1 kilogram at birth.

46. Exela is the holder of approved NDA No. 210660 for cysteine hydrochloride injection, sold under the brand name ELCYS®.

47. Exela's ELCYS® product is labeled to contain no more than 120 mcg/L of aluminum, and is the only FDA approved L-cysteine product available on the market today. [Ex. B (ELCYS® Label), § 11.]

48. The labeling for Exela's ELCYS® product states, "Exposure 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)]." [Id. at § 5.7.]

49. The FDA's Multi-Disciplinary Review and Evaluation for NDA No. 210660 explains the basis for this Warning. [Ex. C (FDA Multi-Disciplinary Review NDA

No. 210660).] First, FDA calculated the maximum daily dose of cysteine in preterm and term infants as 60 mg/kg/day, based on 4 g/kg/day amino acids and 15 mg cysteine/g amino acid (which corresponds to 22 mg ELCYS<sup>®</sup>/g amino acid), as stated in the labeling. Second, FDA identified the volume of ELCYS<sup>®</sup> needed to deliver the 60 mg/kg/day dose of cysteine as 1.76 mL/kg of ELCYS<sup>®</sup>. Multiplying this volume of ELCYS<sup>®</sup> (1.76 mL/kg) by the maximum amount of aluminum in ELCYS<sup>®</sup> (120 mcg/L) results in a maximum exposure of 0.21 mcg/kg/day of aluminum. Thus, FDA concluded: “At the maximum dose in preterm and infants, the aluminum limit of 120 mcg/L will allow a maximum dose of 0.21 mcg/kg/day.” [*Id.* at 65.]

50. In other words, the maximum aluminum exposure amount reported in the ELCYS<sup>®</sup> labeling (0.21 mcg/kg/day) is based specifically on a cysteine injection product that contains no more than 120 mcg/L of aluminum.

51. The FDA’s Multi-Disciplinary Review and Evaluation for NDA No. 210660 shows that FDA treats aluminum as a quality controlled impurity. [*Id.* at 44 (“Currently, without any approved drug products available on the market, marketing approval of a product with quality controlled impurities (i.e., leachables, extractables), especially aluminum exposure, offers a significant benefit.”).]

52. The FDA’s Multi-Disciplinary Review and Evaluation for NDA No. 210660 states:

Since Elcys will be used as a component of TPN, the aluminum content of the drug product is controlled to 120 µg/L (equivalent to 0.0035 µg of aluminum per mg of cysteine) by the drug product specification per recommendation by the Pharm/Tox review team to ensure that infants and pediatric patient exposure to aluminum from the final TPN admixture remains at or below 5 mcg/kg/day per 21 CFR 201.323(e).

[*Id.* at 24.]

53. The FDA’s Multi-Disciplinary Review and Evaluation for NDA No. 210660 states the aluminum content of “other available marketed unapproved or compounded [L-cysteine] products do not meet the regulatory requirements of 21 CFR 201.323 (e). The proposed cysteine product [i.e., ELCYS®] significantly reduces the aluminum content (see Appendix 15.2) and ensures acceptable aluminum exposures in patients receiving this formulation of cysteine hydrochloride.” [*Id.* at 42; *see also id.* at 51-52.]

54. On information and belief, the only “marketed unapproved” cysteine injection product available at the time of the FDA’s Multi-Disciplinary Review and Evaluation statement on April 16, 2019 was the unapproved, high-aluminum L-cysteine product that Sandoz had been marketing since at least 2016. On information and belief, the “other available marketed unapproved” cysteine product to which the FDA was referring was therefore the unapproved, high-aluminum L-cysteine product that Sandoz had been marketing since at least 2016.

55. When FDA approved NDA No. 210660 on April 16, 2019, it applied the aluminum limit for L-cysteine hydrochloride injection products (50 mg/mL) set forth in FDA’s August 4, 2017 letter to Exela.

56. FDA would not have approved NDA No. 210660 if ELCYS® contained more than 145 mcg/L of aluminum at the expiry of its two-year shelf life.

57. 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.” [Ex. B at § 11.]

58. 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%.

59. The FDA-approved labeling for Exela's ELCYS<sup>®</sup> 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.]

60. The FDA-approved labeling for ELCYS<sup>®</sup> 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 labeling and how to administer PN solutions containing ELCYS<sup>®</sup>. [*Id.* at §§ 2.2-2.5.]

61. The FDA-approved labeling for ELCYS<sup>®</sup> 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.* at § 2.4.]

62. The FDA-approved labeling for ELCYS<sup>®</sup> includes the following Warning concerning aluminum toxicity:

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. Tissue loading may occur at even lower rates of administration.

[*Id.* at § 5.7.] The Warning further instructs:

Exposure 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.*]

63. As explained above in paragraphs 49-50, the calculated exposure to aluminum from ELCYS<sup>®</sup> of not more than 0.21 mcg/kg/day referred to in the Warning is based on ELCYS<sup>®</sup> containing no more than 120 mcg/L of aluminum at expiry, as demonstrated by FDA’s calculations. [See Ex. C at 65.]

**B. FDA Approved NOURESS<sup>™</sup>, Another L-Cysteine Hydrochloride Injection Product, With a Limit of 145 mcg/L Aluminum**

64. On December 13, 2019, FDA approved NDA No. 212535 held by Avadel Legacy Pharmaceuticals LLC (“Avadel”) for NOURESS<sup>™</sup> brand cysteine hydrochloride injection USP, 50 mg/mL.

65. The NOURESS<sup>™</sup> Label states that “NOURESS contains no more than 145 mcg/L of aluminum.” [Ex. D (NOURESS<sup>™</sup> Label) at § 11.]

66. The NOURESS<sup>™</sup> Label states, “Exposure to aluminum from NOURESS is not more than 0.25 mcg/kg/day when preterm and neonates are administered the recommended maximum dosage of NOURESS (22 mg cysteine hydrochloride/g of amino acids and 4g of amino acids/kg/day) [*see Dosage and Administration (2.5)*].” [Ex. D at § 5.6.]

67. On information and belief, the calculated exposure to aluminum from NOURESS™ is not more than 0.2552 mcg/kg/day, and is based on NOURESS™ containing no more than 145 mcg/L of aluminum at expiry and, as with ELCYS®, a maximum daily dose of NOURESS™ of 1.76 mL/kg.

68. The FDA's Multi-Disciplinary Review and Evaluation for NDA No. 212535 discloses that in a November 21, 2017 meeting between FDA and Avadel, FDA "[c]larified the requirement regarding aluminum content for L-cysteine product." [Ex. E (FDA Multi-Disciplinary Review NDA No. 212535) at 21.]

69. On information and belief, in the November 21, 2017 meeting between FDA and Avadel, FDA told Avadel that it will not approve L-cysteine hydrochloride injection products (50 mg/ml) that contain more than 145 mcg/L of aluminum during the product's shelf life, consistent with and confirming the aluminum limit FDA set forth in its August 4, 2017 letter to Exela for L-cysteine hydrochloride injection products (50 mg/mL).

70. When FDA approved NDA No. 212535 on December 13, 2019, it applied the no more than 145 mcg/L aluminum limit for L-cysteine hydrochloride injection products (50 mg/mL) set forth in FDA's August 4, 2017 letter to Exela.

71. FDA would not have approved NDA No. 212535 if NOURESS™ contained more than 145 mcg/L of aluminum at the expiry of its two-year shelf life.

72. The FDA's s Multi-Disciplinary Review and Evaluation for NDA No. 212535 explains: "At the maximum cysteine dose in preterm and term infants, the aluminum limit of 145 µg/L will allow a maximum dose of 0.26 µg/kg/day" of aluminum. [Ex. E at 56.]

73. On information and belief, FDA used the same calculation to determine the maximum dose of aluminum of 0.26 µg/kg/day at the maximum dose of NOURESS™ as it did

to calculate the maximum dose of aluminum of 0.21 µg/kg/day at the maximum dose of ELCYS<sup>®</sup>, the only difference being the 145 mcg/L aluminum limit in NOURESS<sup>™</sup> versus the 120 mcg/L aluminum limit in ELCYS<sup>®</sup>.

74. On information and belief, the calculated maximum dose of aluminum of 0.26 µg/kg/day reflected in FDA's Multi-Disciplinary Review and Evaluation for NDA No. 212535 reflects a rounding of the 0.2552 mcg/kg/day value stated in paragraph 67.

75. The FDA's s Multi-Disciplinary Review and Evaluation for NDA No. 212535 expresses FDA's continuing concerns, as of December 2019, about the levels of aluminum in parenteral drug products. For example, FDA stated, "There have been numerous reports of aluminum toxicity resulting from this impurity found in PN [parenteral] solutions over the past three decades. . . . These findings suggest that the total aluminum exposure from prolonged TPN administration to premature infants is a contributing factor to adverse neurologic sequelae and altered bone development and mineralization." [Ex. E at 37.]

76. The FDA's Multi-Disciplinary Review and Evaluation for NDA No. 212535 states that FDA views "21 CFR 301.323 (e) [as] specif[y]ing aluminum concentration limits in large and small volume parenteral products." [Ex. E at 38 (footnotes omitted).]

77. The FDA's Multi-Disciplinary Review and Evaluation for NDA No. 212535 further states the aluminum content of "other available marketed unapproved or compounded [L-cysteine] products do not meet the regulatory requirements of 21 CFR 201.323 (e). The proposed cysteine product [i.e., NOURESS<sup>™</sup>] significantly reduces the aluminum content (see Appendix 15.3) and ensures acceptable aluminum exposures in patients receiving this formulation of cysteine hydrochloride." [Ex. E at 38.]

78. The FDA’s Multi-Disciplinary Review and Evaluation for NDA No. 212535 refers to and provides usage data for a Sandoz “marketed unapproved” cysteine product. [Ex. E at 35 (“Figure 3. Marketed Unapproved (Sandoz Inc) and Approved (Exela Pharma) Usage Data from Jan. 2018-Aug. 2019”).]

79. On information and belief, the only “marketed unapproved” cysteine injection product available at the time of the FDA’s statement in the Multi-Disciplinary Review and Evaluation for NDA No. 212535 in December 2019 was the unapproved, high-aluminum L-cysteine product that Sandoz had been marketing since at least 2016. On information and belief, the “other available marketed unapproved” cysteine product to which FDA was referring was, therefore, the unapproved, high-aluminum L-cysteine product that Sandoz had been marketing since at least 2016.

80. On information and belief, and as demonstrated through FDA’s approvals of the NDAs for ELCYS<sup>®</sup> and NOURESS<sup>™</sup>, FDA will not approve an L-cysteine hydrochloride injection product (50 mg/mL) if it contains more than 145 mcg/L of aluminum during its approved shelf life.

81. On January 7, 2020, Exela filed a patent infringement lawsuit against Avadel asserting the ’453 patent in the United States District Court for the District of Delaware. That lawsuit bears Case Number 1:20-cv-00024-MN and is assigned to Judge Noreika.

**C. Eton Pharmaceutical’s Proposed ANDA for a Generic L-Cysteine Hydrochloride Injection Also Contains Low Aluminum**

82. On or about February 3, 2020, Plaintiff received a letter signed on behalf of Eton Pharmaceuticals, Inc. (“Eton”) (“Eton’s Paragraph IV Letter”).

83. Eton’s Paragraph IV Letter informed Exela that Eton had filed ANDA No. 214082 with the FDA seeking approval for Cysteine Hydrochloride Injection, USP, 500

mg/50 mL (50 mg/mL), 10 mL Fill (“Eton’s ANDA Product”), which is a generic version of Exela’s ELCYS® product.

84. Eton’s Paragraph IV Letter included a detailed statement of Eton’s factual and legal bases for its position that each claim of Exela’s ’453 patent is invalid and/or will not be infringed by the commercial manufacture, use, sale, offer for sale, or importation into the U.S. of Eton’s ANDA Product.

85. Eton’s Paragraph IV Letter does not allege non-infringement for any of the ’453 patent claims based on the aluminum levels of Eton’s ANDA Product, including claim 4 of the ’453 patent, which requires a stable L-cysteine composition with aluminum in an amount from about 1.0 mcg/L to about 150 mcg/L, and claim 5 of the ’453 patent, which further requires the aluminum amount to be from about 1.0 mcg/L to about 100 mcg/L.

86. On March 16, 2020, Exela filed a patent infringement lawsuit against Eton asserting the ’453 and ’153 patents in the United States District Court for the District of Delaware. That lawsuit bears Case Number 1:20-cv-00365-MN and is assigned also to Judge Noreika (the “Eton lawsuit”).

87. On information and belief, including as evidenced by Eton’s Paragraph IV Letter and as alleged in Exela’s Complaint in the Eton lawsuit, Eton’s ANDA Product contains no more than 145 mcg/L of aluminum during its shelf life and will state that on its labeling.

88. On information and belief, FDA will apply to Eton’s ANDA No. 214082 the no more than 145 mcg/L aluminum limit for L-cysteine hydrochloride injection products (50 mg/mL) set forth in FDA’s August 4, 2017 letter to Exela. This limit was enforced by the FDA consistently in approving both ELCYS® and NOURESS™, which are labeled to contain no more than 120 mcg/L and 145 mcg/L of aluminum, respectively, during the products’ shelf life.

89. On information and belief, FDA will not approve ANDA No. 214082 if Eton's ANDA Product contains more than 145 mcg/L of aluminum at the expiry of its shelf life.

90. On information and belief, FDA will not approve any ANDA for an L-cysteine hydrochloride injection product (50 mg/mL) if it contains more than 145 mcg/L of aluminum at the expiry of its shelf life.

**D. The Asserted '453 Patent**

91. On November 19, 2019, the United States Patent and Trademark Office ("USPTO") issued the '453 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 '453 patent is attached to this Complaint as Exhibit F.

92. The '453 patent is assigned to Exela.

93. On November 19, 2019, Exela submitted the '453 patent for listing in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book," which provides notice concerning patents covering FDA-approved drugs.

94. On or about November 20, 2019, the FDA published the '453 patent in the Orange Book.

95. Claim 1 of the '453 patent reads as follows:

A stable L-cysteine composition for parenteral administration, 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;  
Aluminum (Al) in an amount from about 1.0 parts per billion (ppb) to about 250 ppb;  
L-cystine in an amount from about 0.001 wt % to about 2.0 wt % relative to L-cysteine;  
pyruvic acid in an amount from about 0.001 wt % to about 2.0 wt % relative to L-cysteine;  
a pharmaceutically acceptable carrier, comprising water;  
headspace oxygen that is from about 0.5% v/v to 4.0% v/v from the time of manufacture to about 1 month from manufacture when stored at room temperature;

dissolved oxygen present in the carrier in an amount from about 0.1 parts per million (ppm) to about 5 ppm from the time of manufacture to about 1 month from manufacture when stored at room temperature, wherein the composition is enclosed in a single-use container having a volume of from about 10 mL to about 100 mL.

96. Claim 4 of the '453 patent reads as follows:

The composition of claim 1, wherein said Aluminum is present in an amount from about 1.0 ppb to about 150 ppb.

97. Claim 22 of the '453 patent reads as follows:

A method of preparing a reduced Aluminum composition for a total parenteral nutrition regimen comprising L-cysteine, the method comprising:  
mixing a composition comprising L-cysteine and/or a pharmaceutically acceptable salt thereof and/or hydrate thereof comprising:  
Aluminum in an amount from about 1.0 parts per billion (ppb) to about 250 ppb;  
L-cystine in an amount from about 0.001 wt % to about 2.0 wt % relative to L-cysteine; and  
pyruvic acid in an amount from about 0.001 wt % to about 2.0 wt % relative to L-cysteine;  
with a composition comprising one or more amino acids selected from the group consisting of: leucine, isoleucine, lysine, valine, phenylalanine, histidine, threonine, methionine, tryptophan, alanine, arginine, glycine, proline, serine, and tyrosine; and a pharmaceutically acceptable carrier, comprising water, to form a composition for infusion having a volume of about 100 mL to about 1000 mL,  
wherein the Aluminum provided in said parenteral nutrition regimen is from about 1-2 to about 4-5 micrograms/kg/day.

98. Exela's ELCYS<sup>®</sup> product, and its use according to the directions and instructions on the FDA-approved label, is covered by at least claims 1, 4, and 22 of the '453 patent.

**E. The Asserted '155 Patent**

99. 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 G.

100. The '155 patent is assigned to Exela.

101. On March 10, 2020, Exela submitted the '155 patent for listing in the Orange Book, which provides notice concerning patents covering FDA-approved drugs.

102. On or about March 11, 2020, the FDA published the '155 patent in the Orange Book.

103. 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.

104. Claim 3 of the '155 patent reads as follows:

The method of claim 1, wherein said stable L-cysteine composition contributes Aluminum in an amount less than 150 mcg/L.

105. 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%.

106. Exela's ELCYS<sup>®</sup> product, and its use according to the directions and instructions on the FDA-approved label, is covered by at least claims 1, 3, and 27 of the '155 patent.

**ACTS GIVING RISE TO THIS ACTION FOR DEFENDANT’S INFRINGEMENT  
OF THE PATENTS-IN-SUIT**

**A. Receipt of and Representations in Sandoz’s Paragraph IV Letter**

107. On or about [REDACTED], Plaintiff received Sandoz’s Paragraph IV Letter, dated [REDACTED], signed on behalf of Sandoz by Abigail Langsam of the law firm Arnold & Porter Kaye Scholer LLP.

108. Sandoz’s Paragraph IV Letter states that Sandoz had filed with FDA, and FDA had received, ANDA No. 209994 for Cysteine Hydrochloride Injection, USP, 500 mg/10 mL (50 mg/mL) single-dose vials (“Sandoz’s ANDA Product”), which is a generic version of Exela’s ELCYS® product.

109. Sandoz’s Paragraph IV Letter states that ANDA No. 209994 contains the required bioavailability and/or bioequivalence data and/or bioequivalence waiver.

110. Sandoz’s Paragraph IV Letter states that the active ingredient in Sandoz’s ANDA Product is cysteine hydrochloride; the strength of Sandoz’s ANDA Product is equivalent to ELCYS® (50 mg/mL); and the dosage form of Sandoz’s ANDA Product is a solution.

111. Sandoz’s Paragraph IV Letter also states that ANDA No. 209994 “contains a paragraph IV certification to obtain approval to engage in the manufacture, use or sale of Cysteine Hydrochloride Injection USP, 500 mg/10 mL (50 mg/mL) single-dose vials before the expiration of U.S. Patent Nos. 10,478,453 and 10,538,155, which are listed in the Patent and Exclusivity Information Addendum of FDA’s publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (“the Orange Book”) with respect to ELCYS.”

112. This action is being commenced before the expiration of 45 days from the date Exela received Sandoz’s Paragraph IV Letter, which triggers a stay of FDA approval of Sandoz’s ANDA No. 209994 pursuant to 21 U.S.C § 355(j)(5)(B)(iii).

113. Attached to Sandoz's Paragraph IV Letter is a statement of the factual and legal bases for Sandoz's position that the '453 and '155 patents are invalid and/or will not be infringed by the commercial manufacture, use, or sale of Sandoz's ANDA Product.

114. In particular, Sandoz's Paragraph IV letter alleges that claims 1-22 of the '453 patent are not infringed and/or invalid, and that claims 1-30 of the '155 patent are not infringed and/or are invalid.

115. Sandoz's Paragraph IV letter alleges that [REDACTED]

[REDACTED]  
[REDACTED]  
[REDACTED]

116. Sandoz's Paragraph IV letter purports to represent that [REDACTED]

[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]

117. [REDACTED]

[REDACTED]

118. [REDACTED]

[REDACTED]

119. [REDACTED]

[REDACTED]

120. [REDACTED]

[REDACTED]

121. [REDACTED]

[REDACTED]

122. [REDACTED]

[REDACTED]

123. As demonstrated below, [REDACTED]

[REDACTED]

[REDACTED] and Sandoz knows and understands FDA will not approve an L-cysteine hydrochloride injection product (50 mg/mL) that contains more than 145 ppb of Aluminum.

**B. Negotiations Over Sandoz's Offer of Confidential Access**

124. Sandoz's Paragraph IV Letter contains an Offer of Confidential Access to ANDA No. 209994 and other documents (the "OCA").

125. The initial terms of the OCA were not acceptable to Exela.

126. From April 16, 2020 to May 8, 2020 the parties negotiated the terms of the OCA, including the scope of documents Sandoz would produce under the OCA.

127. During those negotiations, Exela repeatedly asked Sandoz to explain the basis for the representation made in Sandoz's Paragraph IV Letter that [REDACTED]

[REDACTED]

██████████ given that FDA required both Exela's and Avadel's L-cysteine injection NDA products be limited to  $\leq 145$  ppb of aluminum. Sandoz never provided an explanation.

128. In its letter of May 1, 2020, Exela further explained “[i]t is therefore our understanding that Sandoz’s ANDA product will need to have aluminum levels at or below 145 mcg/L to receive FDA approval. Yet, in your Paragraph IV letter, you suggest that Sandoz’s ANDA product contains aluminum levels above 145 mcg/L, and perhaps even above 250 mcg/L. If Sandoz has FDA correspondence stating that an L-cysteine injection product with over 145 mcg/L of aluminum is likely to be approved, we would like to see it.” In response, Sandoz agreed only to provide its ANDA and represented that “no additional information responsive to your requests exists outside of the ANDA.”

129. During the negotiations, Exela also repeatedly asked Sandoz whether it had any correspondence with FDA about the aluminum limits for Sandoz’s ANDA Product or for approvable L-cysteine products generally, and on each occasion Exela requested production of such correspondence. In response, Sandoz represented that “no additional information responsive to your requests exists outside of the ANDA,” and agreed in the OCA that, to the extent such documents exist, they would be produced.

130. During the negotiations, Exela also repeatedly requested production of up-to-date stability data for Sandoz’s ANDA Product to understand the aluminum content in Sandoz’s ANDA Product over time. In response, Sandoz represented that “no additional information responsive to your requests exists outside of the ANDA,” and agreed in the OCA that, to the extent such documents exist, they would be produced.

131. On May 8, 2020, Exela signed and returned the latest iteration of the OCA, stating “we understand Sandoz is representing that, if there exists any FDA correspondence that

suggests FDA will approve an L-cysteine injection product containing more than 145 mcg/L of aluminum during the product's shelf life, that correspondence is in the ANDA and will be provided to Exela under the OCA. With that understanding, we have executed the OCA."

132. On May 8, 2020, without comment, Sandoz countersigned and returned a copy of the fully-executed OCA and produced to Exela documents represented by Sandoz to be the complete Sandoz ANDA.

133. Accordingly, on information and belief, to the extent FDA has ever communicated to Sandoz that it will approve an L-cysteine injection product containing over 145 mcg/L of aluminum during the product's shelf life, that correspondence should have been included in the documents Sandoz produced to Exela on May 8, 2020.

134. [REDACTED]

135. Thus, based on information and belief, the laws and regulations regarding generic drugs including FDA's interpretation of 21 C.F.R. § 201.323 as applied to L-cysteine injection products (specifically, FDA's approvals of ELCYS® and NOURESS™), Sandoz's assertions and representations in its Paragraph IV Letter and during the OCA discussions, and Sandoz's ANDA documents produced pursuant to the OCA, Exela alleges, consistent with FDA's mandate that L-cysteine hydrochloride injection products must contain no more than 145 mcg/L of aluminum at expiry to receive FDA approval, that the product for which Sandoz is seeking approval under ANDA No. 209994 will contain no more than 120 mcg/L of aluminum, and thus will infringe one or more claims of the '453 and '155 patents.

**C. Sandoz's ANDA Product**

136. [REDACTED]

137. [REDACTED]

138. [REDACTED]

[REDACTED]

[REDACTED]

139. [REDACTED]

[REDACTED]

[REDACTED] Sandoz responded by alleging that the OCA only applies to [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED], and at no time during the extensive negotiations between the parties about the OCA did Sandoz state any such limitation. Rather, Sandoz represented to Exela that it would produce “a complete and unredacted copy of Sandoz’s ANDA.” Thus, by withholding portions of the ANDA, and communications with FDA about the ANDA and ANDA product, Sandoz is in violation of the terms of the OCA. As such, Exela must resort to the discovery process to obtain this information, along with the other relevant information Sandoz has not yet provided.

140. [REDACTED]

141. On March 13, 2020, FDA notified Sandoz that ANDA No. 209994 had been received, and thus was deemed acceptable for review, as of January 17, 2020.

142. FDA’s decision to receive ANDA No. 209994 reflects FDA’s threshold determination that the application is substantially complete, meaning the ANDA “is sufficiently complete to permit a substantive review.” *See* FDA, Guidance for Industry: ANDA Submissions — Refuse-to-Receive Standards Rev. 2 at p.1 (Dec. 2016).

143. FDA’s decision to receive ANDA No. 209994 does not mean that ANDA No. 209994 is approvable as submitted. *See* 21 C.F.R. §§ 314.101(b)(1), (f)(2); 21 C.F.R. § 314.105(d); 21 C.F.R. § 314.127.

144. In filing and maintaining ANDA No. 209994, Sandoz has requested and continues to request FDA’s approval to market, offer for sale, and sell a generic version of Exela’s ELCYS<sup>®</sup> product throughout the United States, including in the State of Delaware.

145. On information and belief, following FDA approval of ANDA No. 209994, Sandoz will market, offer for sale, and sell the approved generic version of ELCYS<sup>®</sup> throughout the United States, including in the State of Delaware, and Sandoz’s ANDA Product will be prescribed and used throughout the United States, including in the State of Delaware.

146. Sandoz’s effort to seek FDA approval to market a generic version of ELCYS<sup>®</sup> prior to the expiration of the ’453 and ’155 patents constitutes an act of infringement pursuant to 35 U.S.C. § 271(e)(2). It also creates a justiciable controversy between the parties with respect to the subject matter of ANDA No. 209994, the ’453 patent, and the ’155 patent as further evidenced by Sandoz’s Paragraph IV Letter.

147. On information and belief, Sandoz’s ANDA Product will be sold and distributed with labeling that contains substantially the same instructions for use as those in the label for Exela’s ELCYS<sup>®</sup> product, including instructions that are substantially the same as those described above in paragraphs 59-61.

148. For example, on information and belief, and as demonstrated in Sandoz's ANDA, the proposed labeling for Sandoz's ANDA Product, like the labeling for ELCYS<sup>®</sup>, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

149. On information and belief, based on that instruction, which appears in the indications and usage section of the proposed labeling for Sandoz's ANDA Product, [REDACTED]

[REDACTED]

[REDACTED]

150. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

151. On information and belief, and as Sandoz's ANDA demonstrates, [REDACTED]

[REDACTED]

152. On information and belief, Sandoz's ANDA Product is stable and will not be approved by FDA if it is not stable.

153. Sandoz's ANDA Product is an SVP and must comply with 21 C.F.R. § 201.323.

154. On information and belief, Sandoz has been aware that ELCYS<sup>®</sup> is labeled to contain no more than 120 mcg/L of aluminum during its shelf life since on or around April 15, 2019 when FDA approved NDA No. 210660.

155. On information and belief, Sandoz has been aware of FDA's August 4, 2017 letter to Exela, which sets forth the maximum aluminum content for L-cysteine hydrochloride injection

products (50 mg/mL) as no more than 145 mcg/L during the product's shelf life, since at least November 6, 2019, because Exela submitted the letter as an exhibit to the Complaint Exela filed against Sandoz in *Exela Pharma Sciences, LLC v. Sandoz, Inc.*, C.A. No. 1:19-cv-00318 (W.D.N.C.), alleging unfair and deceptive trade practices.

156. On information and belief, Sandoz has been aware that NOURESS™ is labeled to contain no more than 145 mcg/L of aluminum during its shelf life since on or around December 13, 2019 when FDA approved Avadel's NDA No. 212535.

157. On information and belief, Sandoz knew and understood before submitting ANDA No. 209994 to FDA on January 17, 2020, and before FDA deemed ANDA No. 209994 accepted for review on March 13, 2020, that FDA had set a maximum aluminum content for L-cysteine hydrochloride injection products (50 mg/mL) of no more than 145 mcg/L during the product's shelf life, as evidenced by FDA's August 4, 2017 letter to Exela and FDA's approvals of NDA Nos. 210660 (ELCYS®) and 212535 (NOURESS™).

158. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

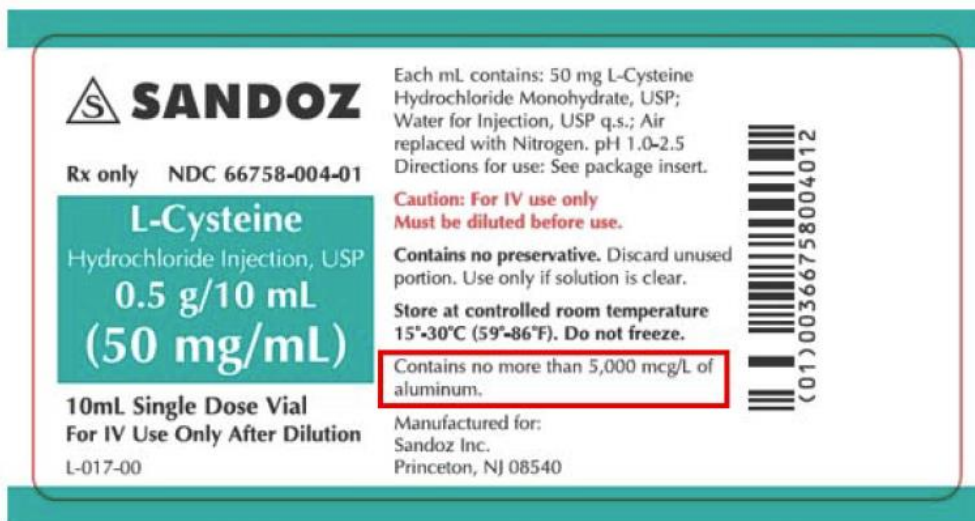
159. On information and belief, Sandoz knows and understands, or should know and understand, that FDA will not approve an ANDA for an L-cysteine hydrochloride injection product (50 mg/mL) that contains more than 145 mcg/L of aluminum during the product's shelf life, including Sandoz's ANDA No. 209994.

160. On information and belief, the ANDA Product that Sandoz will market, offer for sale, and sell upon approval of ANDA No. 209994 will contain no more than 145 mcg/L of

aluminum during the product's shelf life, per FDA's requirements as evidenced by FDA's August 4, 2017 letter to Exela and FDA's approvals of NDA Nos. 210660 (for ELCYS<sup>®</sup>) and 212535 (for NOURESS<sup>™</sup>).

161. Pursuant to 21 C.F.R. § 201.323, all SVPs must state on their immediate container label the maximum amount of aluminum at expiry.

162. On information and belief, Sandoz is aware of this requirement. Indeed, the immediate container label for the unapproved L-cysteine hydrochloride injection product Sandoz sold until October 2019, as noted previously pursuant to FDA's "shortage" program, which purports to permit importation of unapproved drugs during a shortage (or in this case, absence) of an FDA-approved version of the drug in the United States, stated "Contains no more than 5,000 mcg/L of aluminum," as annotated below:



163. In October 2019, FDA ordered Sandoz to immediately stop importation into and distribution in the United States of this unapproved product.

164. In contrast, the proposed container label for Sandoz's ANDA Product [REDACTED]

165. Instead, the proposed container label for Sandoz's ANDA Product simply states:

[REDACTED]

166. The following is a copy of the proposed container label for Sandoz's ANDA Product:

[REDACTED]

167. In contrast, the ELCYS<sup>®</sup> container label states "Contains no more than 120 mcg/L of aluminum."

168. The only purported explanation Sandoz provided in its ANDA for not using the same language in its proposed container label as appears in the container label for ELCYS<sup>®</sup> is

[REDACTED]

169. Sandoz's proposed container label [REDACTED]

[REDACTED]

[REDACTED]

170. Sandoz's proposed package insert for its ANDA Product states in Section 11:

[REDACTED]

171. In contrast, the ELCYS® package insert states in Section 11: "ELCYS contains no more than 120 mcg/L of aluminum."

172. The only purported explanation Sandoz provided in its ANDA for not using the same language in Section 11 of its proposed package insert as appears in the package insert for ELCYS® is [REDACTED]

173. Sandoz's proposed package insert for its ANDA Product states in Section 5.7:

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

174. As explained in paragraphs 48-50 above, the maximum aluminum exposure reported in Sandoz's proposed package insert of [REDACTED]

[REDACTED]

175. [REDACTED]

[REDACTED]

[REDACTED]

176. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] and will therefore infringe one or more claims of the '453 and '155 patents.

177. [REDACTED]

[REDACTED]

178. Sandoz did not produce [REDACTED] to Exela until May 19, 2020, five days after Exela had filed its original Complaint in the present case, 1:20-cv-00645-MN, which necessitates this amendment.

179. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

180. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

181. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

182. [REDACTED]

[REDACTED]

[REDACTED]

183. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

184. On information and belief, and as demonstrated in Sandoz's ANDA, [REDACTED]

[REDACTED]

[REDACTED]

185. On information and belief, Sandoz's ANDA Product therefore contains not more than about 2.0 wt% of cystine relative to L-cysteine and not more than 2.0 wt% pyruvic acid relative to L-cysteine. On information and belief, Sandoz's ANDA Product therefore also contains less than 2.0% of the impurity cystine relative to L-cysteine and less than 2.0% of the impurity pyruvic acid relative to L-cysteine, and from about 0.001 wt % to about 2.0 wt% cystine (or L-cysteine) relative to L-cysteine and from about 0.001 wt % to about 2.0 wt % pyruvic acid relative to L-cysteine. Indeed, Sandoz's Paragraph IV Letter [REDACTED]

[REDACTED]

[REDACTED]

186. On information and belief, Sandoz's ANDA Product contains dissolved oxygen present in the carrier in an amount from about 0.1 ppm to about 5 ppm from the time of manufacture to about 1 month from manufacture when stored at room temperature. Indeed, Sandoz's Paragraph IV Letter [REDACTED]

[REDACTED]

187. On information and belief, Sandoz's ANDA Product contains headspace oxygen that is from about 0.5% v/v to 4.0% v/v from the time of manufacture to about 1 month from

manufacture when stored at room temperature. Indeed, Sandoz's Paragraph IV Letter [REDACTED]  
[REDACTED]

188. On information and belief, and as demonstrated in Sandoz's ANDA, the labeling for Sandoz's ANDA Product, like the labeling for ELCYS<sup>®</sup>, [REDACTED]  
[REDACTED]

[REDACTED] On information and belief, like the labeling for ELCYS<sup>®</sup>, the labeling for Sandoz's ANDA Product [REDACTED]  
[REDACTED]

189. On information and belief, and as demonstrated in Sandoz's ANDA, the label for Sandoz's ANDA Product [REDACTED] [REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]

190. On information and belief, and as demonstrated in Sandoz's ANDA, the labeling for Sandoz's ANDA Product [REDACTED]  
[REDACTED]

[REDACTED] On information and belief, following the instructions on the labeling for Sandoz's ANDA Product results in a parenteral nutrition regimen with aluminum present in an amount from 1-2 to 4-5 micrograms/kg/day.

191. On information and belief, a composition prepared according to the admixture instructions in the labeling for Sandoz's ANDA Product will be used for infusion in a TPN regimen and has a volume of about 100 mL to about 1000 mL.

192. On information and belief, and as demonstrated in Sandoz's ANDA, the labeling for Sandoz's ANDA Product, like the labeling for ELCYS<sup>®</sup>, [REDACTED]

[REDACTED] On information and belief, when used as directed in the labeling, Sandoz's ANDA Product will be dosed to provide a therapeutically effective amount of L-cysteine to patients.

193. On information and belief, the composition of Sandoz's ANDA Product meets all the limitations of at least claims 1 and 4 of the '453 patent, either literally or under the doctrine of equivalents.

194. On information and belief, healthcare providers will admix Sandoz's ANDA Product according to the instructions in Sandoz's labeling and administer those compositions to patients who require TPN.

195. On information and belief, when healthcare providers admix Sandoz's ANDA Product according to the instructions in Sandoz's labeling 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 claim 22 of the '453 patent and claims 1, 3, and 27 of the '155 patent, either literally or under the doctrine of equivalents.

196. Accordingly, on information and belief, healthcare providers that follow the instructions in the labeling for Sandoz's ANDA Product will directly infringe at least some claims of the '453 and '155 patents.

### **COUNT I**

#### **(Infringement of the '453 Patent Under 35 U.S.C. § 271(e)(2))**

197. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

198. Sandoz submitted ANDA No. 209994 to the FDA under section 505(j) of the Federal Food, Drug and Cosmetic Act (“FDCA”) to obtain approval to engage in the commercial manufacture, importation, use, sale, and/or offer for sale of Sandoz’s ANDA Product throughout the United States. By submitting the application, Sandoz has committed an act of infringement of the ’453 patent under 35 U.S.C. § 271(e)(2)(A).

199. The commercial manufacture, importation, use, sale, and/or offer for sale of Sandoz’s ANDA Product will constitute an act of direct infringement of the ’453 patent, either literally or under the doctrine of equivalents.

200. On information and belief, Sandoz became aware of the ’453 patent no later than when it was issued by the USPTO and/or listed in the Orange Book as covering methods of using ELCYS<sup>®</sup>, and no later than when it submitted a Paragraph IV certification to FDA regarding ANDA No. 209994, in which it identified the ’453 patent as a patent covering the approved product ELCYS<sup>®</sup>.

201. On information and belief, Sandoz knew or should have known that its commercial making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of Sandoz’s ANDA Product, with its labeling, will actively induce the direct infringement of the ’453 patent.

202. On information and belief, Sandoz knew or should have known that Sandoz’s ANDA Product will be especially made or especially adapted for use in an infringement of the ’453 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 proposed labeling. And, on information and belief, Sandoz knew or should have known that its commercial offering to sell,

selling, importing, or otherwise distributing of Sandoz's ANDA Product will actively contribute to the direct infringement of the '453 patent.

203. Unless and until Sandoz is enjoined from infringing the '453 patent, Exela will suffer irreparable injury for which damages are an inadequate remedy.

204. Exela 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 approval of Sandoz's ANDA No. 209994 be a date that is not earlier than the expiration date of the '453 patent.

## **COUNT II**

### **(Declaratory Judgment of Infringement of the '453 Patent Under 35 U.S.C. § 271(a))**

205. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

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

207. There is an actual case or controversy such that the Court may entertain Exela'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.

208. On information and belief, Sandoz will engage in the commercial manufacture, use, offer for sale, sale, and/or importation of Sandoz's ANDA Product immediately and imminently upon FDA approval of ANDA No. 209994.

209. Sandoz's actions, including but not limited to, the development of Sandoz's ANDA Product, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Sandoz has made and will continue to make substantial preparation in the United States, including in the State of Delaware, to manufacture, sell, offer to sell, and/or import Sandoz's ANDA Product.

210. On information and belief, Sandoz's ANDA Product practices all limitations of at least claims 1 and 4 of the '453 patent, either literally or under the doctrine of equivalents, as detailed above, and thus the commercial manufacture, importation, use, sale, and/or offer for sale of Sandoz's ANDA Product will constitute an act of infringement of the '453 patent.

211. The commercial manufacture, importation, use, sale, and/or offer for sale of Sandoz's ANDA Product in violation of Exela's patent rights will cause harm to Exela, for which damages are inadequate.

212. Exela is entitled to a declaratory judgment that the future commercial manufacture, use, offer for sale, sale and/or importation of Sandoz's ANDA Product before patent expiration will constitute direct infringement of at least claims 1 and 4 of the '453 patent under 35 U.S.C. § 271(a).

213. Unless and until Sandoz is enjoined from infringing the '453 patent, Plaintiff will suffer irreparable injury for which damages are an inadequate remedy.

### **COUNT III**

#### **(Declaratory Judgment of Infringement of the '453 Patent Under 35 U.S.C. § 271(b))**

214. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

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

216. There is an actual case or controversy such that the Court may entertain Exela'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.

217. Sandoz has actual knowledge of the '453 patent.

218. On information and belief, Sandoz became aware of the '453 patent no later than when it was issued by the USPTO and/or listed in the Orange Book as covering

methods of using ELCYS<sup>®</sup>, and no later than when it submitted a Paragraph IV certification to the FDA regarding ANDA No. 209994, in which it identified the '453 patent as one of the patents covering ELCYS<sup>®</sup>.

219. On information and belief, Sandoz will engage in the commercial manufacture, use, offer for sale, sale, importation or other promotion and/or distribution of Sandoz's ANDA Product immediately and imminently upon FDA approval of ANDA No. 209994.

220. Sandoz's actions, including but not limited to, the development of Sandoz's ANDA Product, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Sandoz has made and will continue to make substantial preparation in the United States, including in the State of Delaware, to manufacture, sell, offer to sell, import or otherwise promote and/or distribute Sandoz's ANDA Product.

221. On information and belief, Sandoz will include within the packaging of its ANDA Product, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claim 22 of the '453 patent.

222. On information and belief, healthcare providers preparing a total parenteral nutrition regimen using Sandoz's ANDA Product within the United States according to the instructions in the product's labeling will directly infringe at least claim 22 of the '453 patent, either literally or under the doctrine of equivalents.

223. On information and belief, Sandoz possesses specific intent to encourage direct infringement of at least claim 22 of the '453 patent, including because Sandoz's labeling for its ANDA Product instructs users to perform the patented method, providing evidence of an affirmative intent to induce infringement. Furthermore, because ELCYS<sup>®</sup> and Sandoz's ANDA

Product have no substantial non-infringing uses, Sandoz intends for the use of its generic version of ELCYS® to directly infringe at least claim 22 of the '453 patent.

224. On information and belief, upon awareness of the '453 patent, Sandoz either actually knew of the potential for infringement of at least claim 22 of the '453 patent, or was willfully blind as to the potential for that infringement, at least, because Sandoz provides instructions for infringement of at least claim 22 of the '453 patent in its proposed product labeling.

225. The commercial making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of Sandoz's ANDA Product, with its labeling, will constitute an act of active inducement of infringement of at least claim 22 of the '453 patent.

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

227. Exela is entitled to a declaratory judgment that the future making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of Sandoz's ANDA Product before patent expiration will constitute active inducement of infringement of at least claim 22 of the '453 patent under 35 U.S.C. § 271(b).

228. Unless and until Sandoz is enjoined from infringing the '453 patent, Exela will suffer irreparable injury for which damages are an inadequate remedy.

#### **COUNT IV**

##### **(Declaratory Judgment of Infringement of the '453 Patent Under 35 U.S.C. § 271(c))**

229. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

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

231. There is an actual case or controversy such that the Court may entertain Exela'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.

232. Sandoz has actual knowledge of the '453 patent.

233. On information and belief, Sandoz became aware of the '453 patent no later than when it was issued by the USPTO and/or listed in the Orange Book as covering ELCYS<sup>®</sup>, and no later than when it submitted a Paragraph IV certification to the FDA regarding ANDA No. 209994, in which it identified the '453 patent as one of the patents covering ELCYS<sup>®</sup>.

234. On information and belief, Sandoz will engage in the commercial manufacture, use, offer for sale, sale, importation and/or other distribution of Sandoz's ANDA Product immediately and imminently upon FDA approval of ANDA No. 209994.

235. Sandoz's actions, including but not limited to, the development of Sandoz's ANDA Product, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Sandoz has made and will continue to make substantial preparation in the United States, including in the State of Delaware, to sell, offer to sell, import, and/or otherwise distribute Sandoz's ANDA Product.

236. On information and belief, Sandoz will include within the packaging of its ANDA Product, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claim 22 of the '453 patent.

237. On information and belief, healthcare providers preparing a total parenteral nutrition regimen using Sandoz's ANDA Product within the United States according to the

instructions in the product's labeling will directly infringe at least claim 22 of the '453 patent, either literally or under the doctrine of equivalents.

238. On information and belief, Sandoz knows that its ANDA Product is a material part of the method of at least claim 22 of the '453 patent, including as evidenced in the contents of its proposed label. On information and belief, Sandoz's ANDA Product was especially made or especially adapted for use by a healthcare provider in a manner that will directly infringe at least claim 22 of the '453 patent, as evidenced in the contents of its proposed labeling. On information and belief, Sandoz's ANDA Product is not a staple article of commerce suitable for substantial non-infringing use, as evidenced by the contents of its proposed 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.

239. Thus, on information and belief, Sandoz will contribute to the infringement of at least claim 22 of the '453 patent in the State of Delaware and elsewhere in the United States by offering to sell, selling, importing, and/or otherwise distributing Sandoz's ANDA Product, which is a material for use in practicing the method of at least claim 22 of the '453 patent.

240. The commercial offering to sell, selling, importing and/or other distribution of Sandoz's ANDA Product for use in practicing the patented method in violation of Exela's patent rights will cause harm to Exela, for which damages are inadequate.

241. Exela is entitled to a declaratory judgment that the future offer for sale, sale, importation and/or other distribution of Sandoz's ANDA Product before patent expiration will constitute contributory infringement of the claims of the '453 patent under 35 U.S.C. § 271(c).

242. Unless and until Sandoz is enjoined from infringing the '453 patent, Exela will suffer irreparable injury for which damages are an inadequate remedy.

**COUNT V**

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

243. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

244. Sandoz submitted ANDA No. 209994 to the FDA under section 505(j) of the FDCA to obtain approval to engage in the commercial manufacture, importation, use, sale, and/or offer for sale of Sandoz's ANDA Product throughout the United States. By submitting the application, Sandoz has committed an act of infringement of the '155 patent under 35 U.S.C. § 271(e)(2)(A).

245. The use of Sandoz's ANDA 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.

246. On information and belief, Sandoz 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 Reference Listed Drugs ("RLDs") serving as the basis for its ANDA submissions, including ELCYS®.

247. On information and belief, Sandoz became aware of the '155 patent no later than when it was issued by the USPTO and/or listed in the Orange Book as covering methods of using ELCYS®.

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

249. On information and belief, Sandoz knew or should have known that Sandoz's ANDA 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 proposed labeling. And, on information and belief, Sandoz knew or should have known that its commercial offering to sell, selling, importing, and/or otherwise distributing of Sandoz's ANDA Product with its labeling will actively contribute to the direct infringement of the '155 patent.

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

251. 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 approval of Sandoz's ANDA No. 209994 be a date that is not earlier than the expiration date of the '155 patent.

## **COUNT VI**

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

252. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

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

254. There is an actual case or controversy such that the Court may entertain Exela'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.

255. Sandoz has actual knowledge of the '155 patent.

256. On information and belief, Sandoz became aware of the '155 patent no later than when it when it was issued by the USPTO and/or listed in the Orange Book as covering methods of using ELCYS<sup>®</sup>, and no later than when it submitted a Paragraph IV certification to the FDA

regarding ANDA No. 209994, in which it identified the '155 patent as one of the patents covering ELCYS®.

257. On information and belief, Sandoz will engage in the commercial manufacture, use, offer for sale, sale, importation or other promotion and/or distribution of Sandoz's ANDA Product immediately and imminently upon FDA approval of ANDA No. 209994.

258. Sandoz's actions, including but not limited to, the development of Sandoz's ANDA Product, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Sandoz has made and will continue to make substantial preparation in the United States, including in the State of Delaware, to manufacture, sell, offer to sell, import or otherwise promote and/or distribute Sandoz's ANDA Product.

259. On information and belief, Sandoz will include within the packaging of its ANDA Product, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claims 1, 3, and 27 of the '155 patent.

260. On information and belief, healthcare providers administering a parenteral nutrition regimen including Sandoz's ANDA Product within the United States according to the instructions in the product's labeling will directly infringe at least claims 1, 3, and 27 of the '155 patent, either literally or under the doctrine of equivalents.

261. On information and belief, Sandoz possesses specific intent to encourage direct infringement of at least claims 1, 3, and 27 of the '155 patent, including because Sandoz's labeling for its ANDA Product instructs users to perform the patented methods, providing evidence of an affirmative intent to induce infringement. Furthermore, because ELCYS® and Sandoz's ANDA Product have no substantial non-infringing uses, Sandoz intends for the

administration of its generic version of ELCYS<sup>®</sup> to directly infringe at least claims 1, 3, and 27 of the '155 patent.

262. On information and belief, upon awareness of the '155 patent, Sandoz either actually knew of the potential for infringement of at least claims 1, 3, and 27 of the '155 patent, or was willfully blind as to the potential for that infringement at least because Sandoz provides instructions for infringement of at least claims 1, 3, and 27 of the '155 patent in its proposed product labeling.

263. The commercial making, using, offering to sell, importing, or otherwise promoting and/or distributing of Sandoz's ANDA Product, with its labeling, will constitute an act of active inducement of infringement of at least claims 1, 3, and 27 of the '155 patent.

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

265. Exela is entitled to a declaratory judgment that the future making, using, offering to sell, importing, or otherwise promoting and/or distributing of Sandoz's ANDA Product before patent expiration will constitute active inducement of infringement of at least claims 1, 3, and 27 of the '155 patent under 35 U.S.C. § 271(b).

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

## **COUNT VII**

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

267. Exela incorporates each of the preceding paragraphs as if fully set forth herein.

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

269. There is an actual case or controversy such that the Court may entertain Exela'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.

270. Sandoz has actual knowledge of the '155 patent.

271. On information and belief, Sandoz became aware of the '155 patent no later than when it was issued by the USPTO and/or listed in the Orange Book as covering methods of using ELCYS<sup>®</sup>, and no later than when it submitted a Paragraph IV certification to the FDA regarding ANDA No. 209994, in which it identified the '155 patent as one of the patents covering ELCYS<sup>®</sup>.

272. On information and belief, Sandoz will engage in the commercial offer for sale, sale, importation and/or other distribution of Sandoz's ANDA Product immediately and imminently upon FDA approval of ANDA No. 209994.

273. Sandoz's actions, including but not limited to, the development of Sandoz's ANDA Product, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Sandoz has made and will continue to make substantial preparation in the United States, including in the State of Delaware, to sell, offer to sell, import, and/or otherwise distribute Sandoz's ANDA Product.

274. On information and belief, Sandoz will include within the packaging of its ANDA Product, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claims 1, 3, and 27 of the '155 patent.

275. On information and belief, healthcare providers administering a parenteral nutrition regimen including Sandoz's ANDA Product within the United States according to the

instructions in the product's labeling will directly infringe at least claims 1, 3, and 27 of the '155 patent, either literally or under the doctrine of equivalents.

276. On information and belief, Sandoz knows that its ANDA Product is a material part of the method of at least claims 1, 3, and 27 of the '155 patent, including as evidenced in the contents of its proposed label. On information and belief, Sandoz's ANDA Product was especially made or especially adapted for use by a healthcare provider in a manner that will directly infringe at least claims 1, 3, and 27 of the '155 patent, as evidenced by the contents of its proposed labeling. On information and belief, Sandoz's ANDA Product is not a staple article of commerce suitable for substantial non-infringing use, as evidenced by the contents of its proposed 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.

277. Thus, on information and belief, Sandoz will contribute to the infringement of the claims of the '155 patent in the State of Delaware and elsewhere in the United States by offering to sell, selling, importing, and/or otherwise distributing Sandoz's ANDA Product, which is a material for use in practicing the method of at least claims 1, 3, and 27 of the '155 patent.

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

279. Exela is entitled to a declaratory judgment that the future offer for sale, sale, importation, and/or other distribution of Sandoz's ANDA Product before patent expiration will constitute contributory infringement of at least claims 1, 3, and 27 of the '155 patent under 35 U.S.C. § 271(c).

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

**PRAYER FOR RELIEF**

WHEREFORE, Plaintiff prays for the following relief:

A. That judgment be issued that Sandoz has infringed the '453 and '155 patents under 35 U.S.C. § 271(e)(2)(A) by submitting ANDA No. 209994 under section 505(j) of the FDCA, and that the commercial manufacture, use, offer to sell, and/or sale within the United States, or importation into the United States, of Sandoz's ANDA Product will constitute an act of infringement of the '453 and '155 patents;

B. That an order be issued under 35 U.S.C. § 271(e)(4)(A) that the effective date of any FDA approval of ANDA No. 209994 shall be a date which is not earlier than the expiration dates of the '453 and '155 patents, as extended by any applicable period of exclusivity;

C. That an injunction be issued under 35 U.S.C. § 271(e)(4)(B) permanently enjoining Sandoz, its officers, agents, servants, employees, licensees, representatives, 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, and/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 '453 or '155 patent;

D. That a declaration be issued under 28 U.S.C. § 2201 that the manufacture, use, offer for sale, sale, and/or importation of Sandoz's ANDA Product before expiration of the '453 and '155 patents does and will infringe the '453 and '155 patents.

E. That an order be issued preliminarily and permanently enjoining Sandoz 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 '453 and '155 patents;

F. If Sandoz engages in the commercial manufacture, use, offer to sell, sale, and/or importation of Sandoz's ANDA Product disclosed in ANDA No. 209994 prior to the expiration of the '453 and '155 patents, as extended by any applicable period of exclusivity, judgment awarding Plaintiff 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;

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

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

I. 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. Specifically, Plaintiff demands a jury trial in the event that there is a launch at risk and damages are in issue.

Dated: May 27, 2020

By: /s/ Robert M. Oakes

Robert M. Oakes (#5217)  
FISH & RICHARDSON P.C.  
222 Delaware Avenue, 17th Floor  
P.O. Box 1114  
Wilmington, DE 19899  
Tel: (302) 652-5070  
oakes@fr.com

OF COUNSEL:

Jonathan E. Singer  
FISH & RICHARDSON P.C.  
12390 El Camino Real  
San Diego, CA 92130  
Tel: (858) 678-5070  
singer@fr.com

Corrin N. Drakulich  
Christina Brown-Marshall  
FISH & RICHARDSON P.C.  
1180 Peachtree St. NE, 21<sup>st</sup> Floor  
Atlanta, GA 30309  
Tel: (404) 892-5005  
drakulich@fr.com  
brown-marshall@fr.com

Elizabeth M. Flanagan (#5891)  
Deanna Reichel  
FISH & RICHARDSON P.C.  
60 South Sixth Street, #3200  
Minneapolis, MN 55402  
Tel: (612) 335-5070  
betsy.flanagan@fr.com  
reichel@fr.com

**ATTORNEYS FOR PLAINTIFF  
EXELA PHARMA SCIENCES, LLC**

**CERTIFICATE OF SERVICE**

I hereby certify that on this 27<sup>th</sup> day of May, 2020, a true and correct copy of the Sealed Amended Complaint was caused to be served via U.S. Mail on the following attorneys:

Abigail Langsam  
Aaron Stiefel  
Arnold & Porter Kaye Scholer LLP  
250 West 55th Street  
New York, NY 10019-9710  
[aaron.stiefel@arnoldporter.com](mailto:aaron.stiefel@arnoldporter.com)  
[abigail.langsam@arnoldporter.com](mailto:abigail.langsam@arnoldporter.com)

/s/ Robert M. Oakes

Robert M. Oakes