IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

EXELA PHARMA SCIENCES, LLC, Plaintiff, v. ETON PHARMACEUTICALS, INC., Defendant.	Civil Action No.: 20-00365-MN **JURY TRIAL DEMANDED**

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"), U.S. Patent No. 10,583,155 ("the '155 patent"), and U.S. Patent No. 10,653,719 ("the '719 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, '155, and '719 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. Plaintiff Exela Pharma Sciences, LLC ("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 Eton Pharmaceuticals, Inc. ("Eton") is a corporation organized and existing under the law of the State of Delaware, having a principal place of business at 21925 West Field Parkway, Suite 235, Deer Park, IL 60010.

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 Eton Pharmaceuticals, Inc. because it is incorporated in Delaware and thus is present in and resides in this District, and because Eton is doing business in this District and thus has purposefully availed itself to the privileges of conducting business in Delaware. On information and belief, Cogency Global Inc., 850 New Burton Road, Suite 201, Dover, Delaware, is Eton's registered agent in Delaware and is authorized to accept service on Eton's behalf.

6. Venue is proper in this District pursuant to 28 U.S.C. § 1400(b) and § 1391 because Eton 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, [Ex. 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 for cysteine hydrochloride injection, sold under the brand name ELCYS®.

14. 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. [Ex. B (ELCYS® Label), § 11.]

15. 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.*]

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

17. 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%.

18. 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®.

19. 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.]

20. 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.]

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