

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ETON PHARMACEUTICALS, INC.,
Petitioner

v.

EXELA PHARMA SCIENCES, LLC,
Patent Owner

Case PGR2020-00068
Patent No. 10,583,155

**PATENT OWNER'S
PRELIMINARY RESPONSE**

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EXHIBIT LIST

| Exhibit No. | Description |
|-------------|---|
| 2001 | Declaration of Dr. Robert J. Kuhn |
| 2002 | Aileen B. Sedman et al., <i>Evidence of Aluminum Loading in Infants Receiving Intravenous Therapy</i> , 312 NEW ENG. J. MED. 1337 (1985) |
| 2003 | Nicholas J. Bishop et al., <i>Aluminum Neurotoxicity in Preterm Infants Receiving Intravenous-Feeding Solutions</i> , 336 NEW ENG. J. MED. 1557 (1997) |
| 2004 | ELCYS [®] Label, Exela Pharma Sciences, LLC |
| 2005 | Amended Complaint (Redacted), <i>Exela Pharma Sciences, LLC v. Sandoz, Inc.</i> , No. 1:20-cv-00645-MN (D. Del. June 1, 2020), ECF No. 12 |
| 2006 | Amended Complaint, <i>Exela Pharma Sciences, LLC v. Eton Pharmaceuticals, Inc.</i> , No. 20-365-MN (D. Del. July 28, 2020), ECF No. 14 |
| 2007 | Declaration of Mark Hartman (Redacted), <i>Exela Pharma Sciences, LLC v. Sandoz Inc.</i> , No. 19-cv-00318-MR (W.D.N.C. Dec. 6, 2019), ECF No. 26-1 |
| 2008 | Megan Fortenberry et al., <i>Evaluating Differences in Aluminum Exposure Through Parenteral Nutrition in Neonatal Morbidities</i> , 9 NUTRIENTS 1249 (2017) |
| 2009 | Kathleen M. Gura, <i>Aluminum Contamination in Parenteral Products</i> , 17 CURR. OPIN. CLIN. NUTR. & METAB. CARE 551 (2014) |
| 2010 | Gordon L. Klein et al., <i>Hypocalcemia Complicating Deferoxamine Therapy in an Infant with Parenteral Nutrition-Associated Aluminum Overload: Evidence for a Role of Aluminum in the Bone Disease of Infants</i> , 9 J. PED. GASTR. & NUTR. 400 (1989) |
| 2011 | Jay M. Mirtallo, <i>Aluminum Contamination of Parenteral Nutrition Fluids</i> , 34 J. PARENTERAL & ENTERAL NUTR. 346 (2010) |
| 2012 | Robert L. Poole et al., <i>Aluminum Exposure From Pediatric Parenteral Nutrition: Meeting the New FDA Regulation</i> , 32 J. PARENTERAL & ENTERAL NUTR. 242 (2008) |
| 2013 | Eton Pharmaceuticals, Inc., Amendment No. 1 to Sales/Marketing Agreement (Form S-1/A, Exhibit 10.18) (Sept. 25, 2018) |

I. INTRODUCTION

Exela's U.S. Patent No. 10,583,155 ("the '155 patent;" Ex. 1001) relates to methods of using stable, highly pure L-cysteine compositions in parenteral nutrition compositions to treat, primarily, preterm and underweight infants by nourishing them during their fragile first days, weeks, or sometimes months of life. While prior L-cysteine compositions contained up to 5,000 ppb¹ of toxic aluminum, the inventive L-cysteine compositions recited in the claims contain no more than 250 ppb of aluminum, and in certain claims even less.² Unlike prior L-cysteine compositions which, as Eton acknowledges, had aluminum levels that were known to increase over time,³ the aluminum and other impurity levels in the

¹ "ppb" is also referred to as "mcg/L" or "µg/L" ("micrograms per Liter").

² *See, e.g.*, Ex. 1001 ('155 Patent) at 58:45-56 (claims 1-3), 60:15-50 (claims 27 and 28); Ex. 1005 (Sandoz Label) at 10.

³ Paper 1 at 34, 42, 51; *see also* Ex. 1008 (Bohrer 2001) at 1 ("[A]nalysis of commercial formulations with and without cysteine" showed that "the contamination is an ongoing process due to the presence of aluminium in glass combined with the affinity of some amino acids for this element."), 4, Table 2 and Fig. 2.

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