IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ADVANCED ACCELERATOR APPLICATIONS, USA, INC., and ADVANCED ACCELERATOR APPLICATIONS, SA, Plaintiffs, v. LANTHEUS MEDICAL IMAGING, INC., LANTHEUS HOLDINGS, INC, Defendants.	)	C.A. No. 24-95 (MN)
ADVANCED ACCELERATOR APPLICATIONS, USA, INC., and ADVANCED ACCELERATOR APPLICATIONS, SA, Plaintiffs, v. CURIUM US LLC, CURIUM US HOLDINGS LLC, CURIUM NETHERLANDS BV, and CURIUM INTERNATIONAL TRADING BV, Defendants.	)	C.A. No. 24-1161 (MN) CONSOLIDATED

MEMORANDUM OPINION

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June 17, 2026
Wilmington, Delaware

NOREIKA, U.S. DISTRICT JUDGE:

This is an action under the Hatch-Waxman Act. Plaintiffs Advanced Accelerator Applications USA, Inc. and Advanced Accelerator Applications SA (together, "ADACAP" or "Plaintiffs") hold patents on manufacturing processes for Lutathera, a cancer treatment containing Lutetium Lu 177 dotatate. Defendants Lantheus Medical Imaging, Inc. and Lantheus Holdings, Inc. (collectively "Lantheus") filed Abbreviated New Drug Application ("ANDA") No. 217060 seeking approval to market a generic version of Lutathera ("Lantheus's Product"). Defendants Curium US LLC, Curium US Holdings LLC, Curium Netherlands BV, and Curium International Trading BV (collectively "Curium") (together with Lantheus, "Defendants") submitted a New Drug Application pursuant to Section 505(b)(2) of the Hatch-Waxman Act seeking approval for a product containing Lutetium Lu 177 dotatate ("Curium's Product").

ADACAP asserts that Lantheus's Product infringes claim 12 of U.S. Patent No. 10,596,276 and claims 3 and 8 of U.S. Patent No. 12,151,003 and that Curium's Product infringes claim 13 of the '276 Patent, claims 3 and 8 of the '003 Patent, claim 6 of U.S. Patent No. 12,168,063, and claims 3, 6, and 15 of U.S. Patent No. 12,161,732 (together, "the Asserted Claims" of the "Asserted Patents"). Curium disputes infringement of all Asserted Claims. Lantheus disputes infringement of claim 12 of the '276 Patent but does not contest infringement of claims 3 and 8 of the '003 Patent. Lantheus and Curium together challenge the validity of all Asserted Claims on multiple grounds.

This Court conducted a five-day bench trial from December 15 through December 19, 2025. (*See* D.I. 338-342[1] ("Tr.")). Post-trial briefing was completed on February 13, 2026. (D.I.

[1] On July 25, 2025, the Court ordered a combined trial on the patent claims asserted in C.A. No. 24-95 (MN) and C.A. No. 24-1161 (MN). To the extent that identical documents were

347, 349, 357, 360, 365, 366). With their briefing, the parties submitted proposed findings of fact. (D.I. 348, 350, 358, 359).

After considering the entire record and applicable law, the Court concludes that (1) Lantheus' Product infringes claims 3 and 8 of the '003 Patent but does not infringe claim 12 of the '276 Patent; (2) Curium's Product does not infringe any of the Asserted Claims and (3) all Asserted Claims are invalid under 35 U.S.C. § 102(a) for being on sale more than one year before the effective filing date of the claimed inventions.[2]

This opinion constitutes the Court's findings of fact and conclusions of law pursuant to Rule 52(a) of the Federal Rules of Civil Procedure.

I. FINDINGS OF FACT ("FF")

A. The Parties

1. Plaintiff Advanced Accelerator Applications USA, Inc. is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at 57 E. Willow Street, Millburn, NJ 07041. (D.I. 309, Ex. 1 ¶ 1).[3]

2. Plaintiff Advanced Accelerator Applications SA is a corporation organized and existing under the laws of France, with its principal place of business in France. (*Id.* ¶ 2).

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filed on both dockets, for simplicity, the Court cites only the docket numbers in C.A. No. 24-95 (MN) in this opinion.

2 At issue in this case are two products accused of infringement, eight claims in four patents, at least five defenses to infringement, and at least six grounds of invalidity. The Court addresses only the issues that suffice to dispose of infringement and validity of the Asserted Claims.

3 The parties agreed that this Court can rely on undisputed facts (D.I. 309, Ex. 1) that the parties jointly submitted before trial. (D.I. 312 at 39:5-20).

3. Defendant Lantheus Medical Imaging, Inc. is a corporation organized and existing under the laws of Delaware, having a principal place of business at 331 Treble Cove Road B300-2, N. Billerica, MA 01862. (*Id.* ¶ 3).

4. Defendant Lantheus Holdings, Inc. is a corporation organized and existing under the laws of Delaware, having a principal place of business at 201 Burlington Road, South Building, Bedford, MA 01730. (*Id.* ¶ 4).

5. Defendant Curium US LLC is a Delaware limited liability company with a principal place of business at 111 West Port Plaza Drive Suite 800, St. Louis, MO 63146. (*Id.* ¶ 5).

6. Defendant Curium US Holdings LLC is a Delaware limited liability company with a principal place of business at 111 West Port Plaza Drive Suite 800, St. Louis, MO 63146. (*Id.* ¶ 6).

7. Defendants Curium Netherlands BV and Curium International Trading BV are both Dutch besloten vennootschaps with a principal place of business at Westerduinweg 3, 1755 LE, Petten, Netherlands. (*Id.* ¶¶ 7, 8).

B. The Witnesses

1. Fact Witnesses

8. Edward Porter, an employee of Curium, testified by deposition at trial. (Tr. 181:24-182:1, Tr. 185:5-8 [Porter]).

9. Phillip DeNoble, the Vice President of Regulatory Affairs and Pharmacovigilance at Lantheus, testified by deposition at trial. (Tr. 182:15-25 [DeNoble]).

10. Simon Robinson testified live at trial. (Tr. 187:13-20 [Robinson]). Dr. Robinson is the former vice president of Research and Pharmaceutical Development at Lantheus and worked at Lantheus for twenty-five years. (Tr. 188:11-189:8 [Robinson]). Dr. Robinson was involved in the due diligence for Lantheus's Product and was a part of a team "that reviewed the data that was

being generated and helped make some decisions about how to improve some of the steps in the manufacturing and what sorts of studies one should do." (Tr. 190:5-191:10 [Robinson]).

11. Stephen Morrissey, currently the Executive Managing Editor of the New England Journal of Medicine, testified by deposition at trial. (Tr. 255:19-256:24 [Morrissey]).

12. Paola Aimone, the senior global program clinical head at Novartis, testified live at trial. (Tr. 263:19-264:5 [Aimone]).

13. Francesco de Palo, an ADACAP employee and a co-inventor of the Asserted Patents, testified by deposition at trial. (Tr. 275:24-276:3 [de Palo]; JTX-0001).

14. Amanda Donovan testified live at trial. (Tr. 359:24-360:6 [Donovan]). Dr. Donovan is the "senior director of research and development at Curium." (Tr. 360:10-14 [Donovan]). Her team was "responsible for formulation development and process design" for Curium's Product. (Tr. 360:24-361:2 [Donovan]).

15. Timothy Witkowski, the global head of Chemistry Patents at Novartis, testified by deposition at trial. (Tr. 392:15-21 [Witkowski]).

16. Clementina Brambati, also an ADACAP employee and a named inventor on the Asserted Patents, testified by deposition at trial. (Tr. 396:5-10 [Brambati]; JTX-0001).

17. Jack Erion testified by deposition at trial. (Tr. 488:10 [Erion]). Dr. Erion is a former President of ADACAP and a co-author of the Strosberg article published in the New England Journal of Medicine. (Tr. 488:4-6 [Erion]; DTX-00062.0001).

18. Francois Nader. a member of ADACAP's Board of Directors from May 2016 until January 2018, testified by deposition at trial. (Tr. 520:4-19 [Nader]).

19. Donato Barbato, another of the named inventors of the Asserted Patents testified by deposition at trial. (Tr. 638:11-15 [Barbato]; JTX-0001). Mr. Barbato began working at

ADACAP in 2009 and began working on Lutetium Lu 177 dotatate around 2013. (Tr. 638:16-24 [Barbato]).

2. ADACAP's Expert Witnesses

20. Eric Price testified live at trial. (Tr. 60:14-21, 700:15-23 [Price]). The Court recognized Dr. Price as an "expert in radiopharmaceuticals." (Tr. 65:9-12 [Price]). Dr. Price is an associate professor in the Department of Chemistry and the Department of Biomedical Engineering at the University of Saskatchewan. (Tr. 62:21-63:10 [Price]). He has experience researching the synthesis and design of new chelators and peptides, modifying peptides, and developing these compounds into radioligands for medical applications, including work with more than ten different radiometals. (Tr. 61:17-62:13, 62:21-63:10 [Price]).

21. David Edwards testified live at trial. (Tr. 110:5-18, 787:11-18 [Edwards]). The Court recognized Dr. Edwards as an expert in the "field of radiopharmaceuticals and the process of manufacturing radiopharmaceuticals." (Tr. 113:22-114:1 [Edwards]). Dr. Edwards has worked on several radiopharmaceuticals that became commercial products and has been an inventor on a number of patents that relate to novel radiopharmaceuticals. (Tr. 113:14-21 [Edwards]). Dr. Edwards is currently an independent drug development consultant. (Tr. 112:22-113:7 [Edwards]).

22. Alison Dennis testified live at trial. (Tr. 640:10-22 [Dennis]). The Court recognized Ms. Dennis as an expert in "European and United Kingdom regulatory pharmaceutical pathways including the specials route in the United Kingdom." (Tr. 643:18-644:10 [Dennis]). Ms. Dennis has been a solicitor in the United Kingdom since 1996 and has practiced in the area of advising medical device and pharmaceutical companies on the regulation and commercialization of their products for twenty-five years. (Tr. 641:19-642:13 [Dennis]). Ms. Dennis is currently a partner at Taylor Wessing LLP based in London. (Tr. 641:16-18 [Dennis]).

23. Takamasa Horio testified live at trial in Japanese with the assistance of an interpreter. (Tr. 660:21-661:13 [Horio]). The Court recognized Mr. Horio as an expert "in Japanese pharmaceutical regulation." (Tr. 663:23-664:3 [Horio]). Mr. Horio has been a practicing lawyer in Japan for about fifteen years and is currently a partner at Mori Hamada & Matsumoto, an international law firm in Japan. (Tr. 662:9-16 [Horio]).

24. Anne Cropp testified live at trial. (Tr. 672:10-18 [Cropp]). The Court recognized Dr. Cropp as an "industry expert on compassionate use programs." (Tr. 676:19-23 [Cropp]). Dr. Cropp has worked in the area of compassionate use for more than thirty years, including at Pfizer, and has worked with more than sixty compassionate use drugs during that time. (Tr. 674:17-675:4; 676:6-10 [Cropp]). Dr. Cropp's experience has made her familiar with the regulatory frameworks concerning compassionate use programs in both the U.S. and Europe. (Tr. 676:11-18 [Cropp]). Dr. Cropp is currently a consultant on compassionate use programs. (Tr. 673:4-7 [Cropp]).

25. James Malackowski testified live at trial. (Tr. 731:1-8 [Malackowski]). The Court recognized Mr. Malackowski as an expert in "accounting and technology licensing and the valuation of technology companies including in the pharmaceutical industry." (Tr. 735:20-736:1 [Malackowski]). Mr. Malackowski is currently the Chief Intellectual Property Officer at J.S. Held, a large technical and risk consultancy, and he is also the Co-Founder, Founding Chairman, and Senior Managing Director for Ocean Tomo, an intellectual property advisory business, where he has responsibility for all divisions of the company. (Tr. 731:13-733:1 [Malackowski]).

3. Defendants' Expert Witnesses

26. Hugh Smyth testified live at trial. (Tr. 208:4-10 [Smyth]). The Court recognized Dr. Smyth as an expert in the field of "pharmaceutical drug product and drug development." (Tr. 212:10-15 [Smyth]). Dr. Smyth is currently a professor in the College of Pharmacy at the

University of Texas and has been a professor there for the past sixteen years. (Tr. 209:17-22 [Smyth]). Dr. Smyth's primary field of teaching and research is pharmaceutical formulation science, including radiopharmaceuticals and radiolabeled compounds. (Tr. 210:3-211:6 [Smyth]). Over the course of his career, Dr. Smyth has taught courses in advanced pharmaceutical manufacturing and pharmaceutics. (Tr. 210:5-11 [Smyth]).

27. Hanford Yau testified live at trial. (Tr. 281:13-21 [Yau]). The Court recognized Dr. Yau as an expert in the field of endocrinology. (Tr. 285:21-286:1 [Yau]). Dr. Yau is board certified in endocrinology, diabetes, metabolism, and internal medicine. (Tr. 283:21-24 [Yau]). Dr. Yau is currently employed as a staff endocrinologist as the Division Chief at the Orlando Veteran Affairs Medical Center, as well as the Associate Program Director and Site Director of fellowship training in endocrinology, diabetes, and metabolism. (Tr. 284:1-8 [Yau]). Dr. Yau also served in the United States Navy Medical Corps from 2005 to 2012, where he received multiple commendations. (Tr. 284:11-18 [Yau]).

28. Adrian Nunn testified live at trial. (Tr. 303:10-15 [Nunn]). The Court recognized Dr. Nunn as an expert in the field of radiopharmaceuticals and their preparation. (Tr. 308:8-12 [Nunn]). Dr. Nunn has academic and industry experience focusing on radiopharmaceutical research and development, diagnostic imaging agents, technetium-based compounds, FDA regulatory submissions, and pharmaceutical manufacturing and control. (Tr. 305:2-306:21 [Nunn]). Dr. Nunn is a member of the Royal Society of Chemistry, the Society of Nuclear Medicine and Molecular Imaging and the Society of Nuclear Medicine FDA Task Force. (Tr. 307:21-308:7 [Nunn]). Dr. Nunn is a named inventor on 42 patents related to radiopharmaceuticals and medical imaging. (Tr. 306:11-307:8 [Nunn]).

29. Dana Trexler testified live at trial. (Tr. 341:4-17 [Trexler]). The Court recognized Ms. Texler as an expert in "economic analysis including objective indicia of nonobviousness with respect to economic success and nexus." (Tr. 343:8-14 [Trexler]). Ms. Trexler is a Managing Director at Stout, a consulting firm, where she co-leads the national intellectual property disputes and valuation practice. (Tr. 341:21-24 [Trexler]). Ms. Trexler is also a certified public accountant and is certified in financial forensics. (Tr. 342:6-9 [Trexler]).

30. David Dick testified live at trial. (Tr. 397:3-13 [Dick]). The Court recognized Dr. Dick as an expert in the field of "radiopharmaceuticals, including radiopharmaceutical development and manufacturing." (Tr. 402:23-403:3 [Dick]). Dr. Dick earned a master's degree and Ph.D. in medical physics and, after serving as head of Cyclotron Physics at Stanford, is now a clinical professor of radiology in the Department of Nuclear Medicine and a clinical professor of pharmaceutical sciences and experimental therapeutics at the University of Iowa. (Tr. 397:18-398:13 [Dick]). Dr. Dick is also chief of radionuclide production and positron emission tomography radiochemistry at the University of Iowa. (Tr. 399:24-400:6 [Dick]).

31. Georgios Skiniotis testified live at trial. (Tr. 491:21-492:3 [Skiniotis]). The Court recognized Dr. Skiniotis as an expert in "structural biology and receptor peptide binding." (Tr. 496:4-9 [Skiniotis]). Dr. Skiniotis has a Ph.D. in structural biology from the European Molecular Biology Lab in Germany. (Tr. 492:25-493:6 [Skiniotis]). He is a faculty member at St. Jude Children's Research Hospital, where he runs an academic laboratory. (Tr. 492:10-17 [Skiniotis]). Previously, he was a professor at Stanford University and the University of Michigan. (Tr. 492:18-24 [Skiniotis]).

32. Debra Litwak testified live at trial. (Tr. 530:7-16 [Litwak]). The Court recognized Dr. Litwak as an expert in "the pharmaceutical industry and expanded access programs." (Tr.

532:21-25 [Litwak]). Dr. Litwak received a degree from the University of Southern California and has worked in the pharmaceutical industry for more than thirty years. (Tr. 530:21-531:7 [Litwak]). She currently owns a consulting company called VitalEdge Healthcare Consulting. (Tr. 530:21-25 [Litwak]). She previously worked at Bristol-Myers Squibb, Amgen, Secura Bio, and BeOne Medicines. (Tr. 531:8-20 [Litwak]). She has been involved in expanded access programs throughout her career and began focusing more heavily on expanded access programs in 2019. (Tr. 532:11-17 [Litwak]).

33. Christopher Bravery testified live at trial. (Tr. 564:19-565:1 [Bravery]). The Court recognized Dr. Bravery "as an expert in regulatory frameworks and the market for unlicensed medicines in the United Kingdom." (Tr. 567:9-15 [Bravery]). Dr. Bravery is a consultant who provides advice to companies developing medicinal products, including advice on regulations and the sale of unlicensed medicines in the United Kingdom. (Tr. 566:22-567:5 [Bravery]). Dr. Bravery has operated his own consultancy business for the past sixteen years. (Tr. 565:22-566:9 [Bravery]). Before becoming a consultant, he worked at the Medicines and Healthcare products Regulatory Agency in the United Kingdom. (Tr. 565:22-566:12 [Bravery]).

34. Ryan Sullivan testified live at trial. (Tr. 601:2-10 [Sullivan]). The Court recognized Dr. Sullivan as an expert in "the economics of life sciences." (Tr. 602:25-603:4 [Sullivan]). Dr. Sullivan is a Managing Director of Secretariat Advisors. (Tr. 601:15-16 [Sullivan]). As a professional economist, Dr. Sullivan advises companies primarily in the areas of licensing, valuation, and business modeling, and serves as an expert in litigation and disputes, spending a significant amount of time in the life sciences. (Tr. 602:4-12 [Sullivan]). Dr. Sullivan has a Ph.D. in Economics from the University of California in San Diego. (Tr. 601:24-602:3 [Sullivan]).

C. The Asserted Patents

35. Plaintiff Advanced Accelerator Applications SA is the assignee and current owner of all Asserted Patents. (D.I. 309, Ex. 1 ¶¶ 14, 19, 24, 29).

36. All Asserted Patents are listed for Lutathera in the FDA's official publication of approved drug products, known as the Orange Book. The '276 Patent was listed on April 13, 2020; the '003 Patent was listed on November 26, 2024; the '732 Patent was listed on December 10, 2024; and the '063 Patent was listed on December 17, 2024. (*Id.* ¶¶ 12, 17, 22, 27).

37. The named inventors of the Asserted Patents are Donato Barbato, Clementina Brambati, Daniela Chicco, Francesco de Palo, Lorenza Fugazza, Maurizio Mariani, and Giovanni Tesoriere. (JTX-0001; JTX-0006-0008).

38. The Asserted Patents share a common specification.[4] (*See id.*).

39. Broadly speaking, the Asserted Patents claims manufacturing processes for a radiopharmaceutical product, which contains Lutetium Lu 177 dotatate (like Lutathera), with sufficient stability to extend the shelf life.

40. Lutathera is indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors in adults. (D.I. 309, Ex. 1 ¶ 32).

41. Lutathera is an injection for intravenous administration containing the active ingredient Lutetium Lu 177 dotatate (sometimes written as ^{177}Lu-Dotatate) – a radioactive compound that rapidly decays over time. (*Id.* ¶ 33; Tr. 477:7-12 [Dick], 66:21-67:21 [Price]).

42. Before Lutathera, hospitals had to prepare Lutetium Lu 177 dotatate drugs on-site and then quickly administer them to patients – a sort of "bedside mix." (Tr. 67:11-18 [Price]).

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[4] Unless specified, the Court cites only to the specification of the '276 Patent when discussing disclosures of the Asserted Patents.

Plaintiffs developed methods of inhibiting the decay of Lutetium Lu 177 dotatate – creating "ready to use" drugs that last longer and can be shipped to distant hospitals. (Tr. 67:22-68:18).

43. ADACAP holds the New Drug Application No. 208700 for Lutathera, which was approved by the FDA on January 26, 2018. (D.I. 309, Ex. A ¶ 34).

1. The '276 Patent

44. The '276 Patent is titled "Stable, Concentrated Radionuclide Complex Solutions" and issued on March 24, 2020. (JTX-0001.0001).

45. The '276 Patent issued from application No. 16/175,261 ("the '261 Application") filed October 30, 2018, which is a continuation-in-part application of application No. 16/140,962 filed September 25, 2018, which in turn is a continuation-in-part of application No. 16/045,484 filed July 25, 2018. (D.I. 309, Ex. 1 ¶ 15).

46. ADACAP asserts claim 12 of the '276 Patent against Lantheus and claim 13 of the '276 Patent against Curium. These claims depend from unasserted claims 1 and 2, which recite:

> 1. A process for manufacturing a pharmaceutical aqueous solution, comprising:
>
> providing a solution comprising a complex of the radio-nuclide ^{177}Lu (Lutetium-177) and a somatostatin receptor binding peptide linked to the chelating agent DOTA; a first stabilizer against radiolytic degradation, and optionally a second stabilizer against radiolytic degradation different from the first stabilizer; and
>
> diluting the solution comprising the complex with an aqueous dilution solution comprising at least one stabilizer against radiolytic degradation to obtain the pharmaceutical aqueous solution;
>
> wherein if the solution comprising the complex comprises only the first stabilizer as an stabilizer against radiolytic degradation and not the second stabilizer, then the aqueous dilution solution comprises at least one stabilizer against radiolytic degradation that is different from the first stabilizer, and in the obtained pharmaceutical aqueous solution, the radionuclide ^{177}Lu is present in a concentration that it provides a volumetric radioactivity of from 250 to 500 MBq/mL and the stabilizers are present in a total concentration of from 1.0 to 5.0 mg/mL, and ethanol is present in a concentration of less than 1%.

(JTX-0001.0021).

2. The process according to claim 1, comprising:

(1) forming a complex of the radionuclide ^{177}Lu and a somatostatin receptor binding peptide linked to the chelating agent DOTA by

(1.1) providing an aqueous solution comprising the radionuclide;

(1.2) providing an aqueous solution comprising the a somatostatin receptor binding peptide linked to the chelating agent, and a first stabilizer against radiolytic degradation and optionally a second stabilizer against radiolytic degradation different from the first stabilizer; and

(1.3) mixing the solutions provided in steps (1.1) and (1.2) and heating the resulting mixture to form a solution comprising the complex;

(2) diluting the solution comprising the complex obtained by step (1) by

(2.1) providing an aqueous dilution solution comprising at least one stabilizer against radiolytic degradation; and

(2.2.) mixing the solution comprising the complex obtained by step (1) with the dilution solution provided in step (2.1) to obtain the pharmaceutical aqueous solution;

wherein if the solution in step (1.2) comprises only one stabilizer that is the first stabilizer, then the solution in step (2.1) comprise at least one stabilizer that is different from the first stabilizer.

(*Id.*).

47. Claim 12 recites:

The process according to claim 2, wherein in step (1.3) the resulting mixture is heated to a temperature of from 70 to 99° C., for from 2 to 59 min.

(*Id.*).

48. Claim 13 recites:

The process according to claim 12, wherein in step (1.3) the resulting mixture is heated to a temperature of from 90 to 98° C. for from 5 to 15 min.

(*Id.*).

2. The '003 Patent

49. The '003 Patent is titled "Stable, Concentrated Radionuclide Complex Solutions" and issued on November 26, 2024. (JTX-0008.0001).

50. The '003 Patent issued from application No. 18/640,884 filed April 19, 2024, which is a continuation of application No. 18/494,042 filed October 25, 2023, which in turn is a continuation of application No. 16/827,606 filed March 23, 2020, which in turn is a continuation of application No. 16/175,261 filed October 30, 2018, which in turn is a continuation-in-part application of application No. 16/140,962 filed September 25, 2018, which in turn is a continuation-in-part of application No. 16/045,484 filed July 25, 2018. (D.I. 309, Ex. 1 ¶ 20).

51. ADACAP asserts claims 3 and 8 of the '003 Patent against both Curium and Lantheus. These claims depend from unasserted claim 1, which recites:

> A pharmaceutical aqueous solution comprising:
>
> (a) a complex comprising (ai) the radionuclide ^{177}Lu, and (aii) a somatostatin receptor binding peptide linked to the chelating agent DOTA; and
>
> (b) at least one stabilizer(s) against radiolytic degradation; wherein: the at least one stabilizer(s) against radiolytic degradation is/are present in a total concentration of 0.5 mg/mL to 10.0 mg/mL; the activity of the pharmaceutical aqueous solution is 7.4 GBq ±10%; the volume of the pharmaceutical aqueous solution is 10 mL to 50 mL; and the pharmaceutical aqueous solution comprises less than 1% ethanol.

(JTX-0008.0023).

52. Claim 3 recites:

> The pharmaceutical aqueous solution of claim 1, wherein the pharmaceutical aqueous solution is a ready-to-use single dose pharmaceutical aqueous solution.

(*Id.*).

53. Claim 7 recites:

> The pharmaceutical aqueous solution of claim 1, wherein the somatostatin receptor binding peptide and the chelating agent form together a molecule selected from DOTA-OC, DOTA-TOC (edotreotide), DOTA-NOC, DOTA-TATE (oxodotreotide), DOTA-LAN, DOTA-VAP, and Satoreotide tetraxetan.

(*Id.*).

54. Claim 8 recites:

> The pharmaceutical aqueous solution of claim 7, wherein the somatostatin receptor binding peptide and the chelating agent form together DOTA-TATE (oxodotreotide).

(*Id.*).

3. The '732 Patent

55. The '732 Patent is titled "Stable, Concentrated Radionuclide Complex Solutions" and issued on December 10, 2024. (JTX-0007.0001).

56. The '732 Patent issued from application No. 18/640,907 filed April 19, 2024, which was is a continuation of application No. 18/494,042 filed October 25, 2023, which in turn is a continuation of application No. 16/827,606 filed March 23, 2020, which in turn is a continuation of application No. 16/175,261 filed October 30, 2018, which in turn is a continuation-in-part application of application No. 16/140,962 filed September 25, 2018, which in turn is a continuation-in-part of application No. 16/045,484 filed July 25, 2018. (D.I. 309, Ex. 1 ¶ 25).

57. ADACAP asserts claims 3, 6 and 15 of the '732 Patent against Curium. Each of these claims depends from unasserted claim 1, which contains the disputed claim limitation relevant to infringement. Claim 1 recites:

> A process for manufacturing a pharmaceutical aqueous solution, the process comprising diluting an aqueous complex solution with an aqueous dilution solution to form the pharmaceutical aqueous solution;
>
> wherein the aqueous complex solution comprises: (a) a complex comprising (ai) the radionuclide ^{177} Lu (Lute-tium-177) and (aii) a somatostatin receptor binding peptide linked to the chelating agent DOTA, and (b) at least one stabilizer(s) against radiolytic degradation; and
>
> wherein the aqueous dilution solution comprises at least one stabilizer(s) against radiolytic degradation which comprises ascorbic acid or a salt thereof;
>
> wherein the radionuclide is present in the pharmaceutical aqueous solution in a concentration that provides a volumetric radioactivity of 250 to 500 MBq/mL, and the stabilizer(s) against radiolytic degradation is/are present in the pharmaceutical aqueous solution in a total concentration of 0.5 mg/mL to 10.0 mg/ml;

wherein the radiochemical purity of the pharmaceutical aqueous solution as determined by HPLC can be maintained at ≥95% for at least 72 hours when stored at 25° C.; and the pharmaceutical aqueous solution comprises less than 2% ethanol.

(JTX-0007.0023).

58. Claim 3 recites:

The process of claim 1, wherein the at least one stabilizer(s) against radiolytic degradation is/are present in a total amount of 15 mg/mL to 50 mg/ml in the aqueous complex solution.

(*Id.*).

59. Claim 4 recites:

The process of claim 1, wherein the somatostatin receptor binding peptide and the chelating agent form together a molecule selected from DOTA-OC, DOTA-TOC (edotreotide), DOTA-NOC, DOTA-TATE (oxodotreotide), DOTA-LAN, DOTA-VAP, and Satoreotide tetraxetan.

(*Id.*).

60. Claim 5 recites:

The process of claim 4, wherein the somatostatin receptor binding peptide and the chelating agent form together a molecule selected from DOTA-TOC (edotreotide), DOTA-TATE (oxodotreotide) and Satoreotide tetraxetan.

(*Id.*).

61. Claim 6 recites:

The process of claim 5, wherein the somatostatin receptor binding peptide and the chelating agent form together DOTA-TATE (oxodotreotide).

(*Id.*).

62. Claim 7 recites:

A pharmaceutical aqueous solution manufactured by the process of claim 1.

(*Id.*).

63. Claim 15 recites:

> The pharmaceutical aqueous solution of claim 7, wherein the pharmaceutical aqueous solution is a ready-to-use single dose pharmaceutical aqueous solution or is pro-vided in numerous dose units.

(*Id.*).

4. The '063 Patent

64. The '063 Patent is titled "Stable, Concentrated Radionuclide Complex Solutions" and issued on December 17, 2024. (JTX-0006.0001).

65. The '063 Patent issued from application No. 18/640,917 filed April 19, 2024, which is a continuation of application No. 18/494,042 filed October 25, 2023, which in turn is a continuation of application No. 16/827,606 filed March 23, 2020, which in turn is a continuation of application No. 16/175,261 filed October 30, 2018, which in turn is a continuation-in-part application of application No. 16/140,962 filed September 25, 2018, which in turn is a continuation-in-part of application No. 16/045,484 filed July 25, 2018. (D.I. 309, Ex. 1 ¶ 30).

66. ADACAP asserts claim 6 of the '063 Patent against Curium. Claim 6 depends from claim 1, which again claims the disputed limitation relevant to infringement. Claim 1 recites:

> A process for manufacturing a pharmaceutical aqueous solution, the process comprising diluting an aqueous complex solution with an aqueous dilution solution to form the pharmaceutical aqueous solution;
>
> wherein the aqueous complex solution comprises: (a) a complex comprising (ai) the radionuclide ^{177}Lu (Lutetium-177) and (aii) a somatostatin receptor binding peptide linked to the chelating agent DOTA, and (b) at least one stabilizer(s) against radiolytic degradation that is/are present in a total concentration of 15 mg/mL to 50 mg/mL in the aqueous complex solution; and
>
> wherein the aqueous dilution solution comprises at least one stabilizer(s) against radiolytic degradation; and
>
> wherein the radionuclide is present in the pharmaceutical aqueous solution in a concentration that provides a volumetric radioactivity of 250 to 500 MBq/mL, and the stabilizer(s) against radiolytic degradation is/are present in the pharmaceutical aqueous solution in a total concentration of 0.5 mg/mL to 10.0 mg/mL; and

the pharmaceutical aqueous solution comprises less than 1% ethanol.

(JTX-0006.0022-23).

67. Claim 4 recites:

> The process of claim 1, wherein the somatostatin receptor binding peptide and the chelating agent form together a molecule selected from DOTA-OC, DOTA-TOC (edotreotide), DOTA-NOC, DOTA-TATE (oxodotreotide),DOTA-LAN, and DOTA-VAP, and Satoreotide tetraxetan.

(*Id.* at 23).

68. Claim 5 recites:

> The process of claim 4, wherein the somatostatin receptor binding peptide and the chelating agent form together a molecule selected from DOTA-TOC (edotreotide), DOTA-TATE (oxodotreotide) and Satoreotide tetraxetan.

(*Id.*).

69. Claim 6 recites:

> The process of claim 5, wherein the somatostatin receptor binding peptide and the chelating agent form together DOTA-TATE.

(*Id.*).

D. Claim Constructions

1. Earlier Claim Construction

70. In a Memorandum Order dated August 13, 2025, the Court construed the following disputed claim terms that are relevant to this Memorandum Opinion:

> "stabilizer[(s)] against radiolytic degradation" means "an agent which protects organic molecules from degradation due to radioactivity."
>
> "the stabilizers . . . in a total concentration of [1.0 to 5.0 mg/mL or 0.5 to 10.0 mg/mL]" in claim 1 of all Asserted Patents means "the first stabilizer, the second stabilizer, and the at least one stabilizer to

the extent present add up to a concentration of [1.0 to 5.0 mg/mL or 0.5 to 10.0 mg/mL]."[5]

(D.I. 250 at 3).

2. Additional Claim Construction Dispute

71. The parties dispute the meaning of "pharmaceutical aqueous solution."

72. ADACAP proposes that the term "pharmaceutical aqueous solution" means "a drug product ready for commercial use," where "for commercial use" is defined in the specification of the Asserted Patents to mean: "the drug product, e.g. a pharmaceutical aqueous solution, is able to obtain (preferably has obtained) marketing authorization by health authorities, e.g. USFDA or EMA, by complying with all drug product quality and stability requirements as demanded by such health authorities, is able to be manufactured (preferably is manufactured) from or at a pharmaceutical production site at commercial scale followed by a quality control testing procedure, and is able to be supplied (preferably is supplied) to remotely located end users, e.g. hospitals or patients." (D.I. 357 at 27; Tr. 117:19-118:11 [Edwards]; JTX-0001.0019; D.I. 348 ¶ 23).

73. Defendants contend that "pharmaceutical aqueous solution" should be given its plain and ordinary meaning, i.e., "a water-based mixture containing an active drug component," where a drug component is something that "can be used as a medicine or for medicinal purposes," based on intrinsic evidence and the testimony of Dr. Dick and Dr. Nunn. (Tr. 315:15-25 [Nunn], Tr. 422:24-423:10 [Dick]; D.I. 349 at 2).

74. Neither the intrinsic nor the extrinsic evidence supports ADACAP's proposed definition that a "pharmaceutical aqueous solution" requires a drug suitable for commercial use and approvable by regulators.

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[5] The Court excluded ethanol as being a stabilizer under this construction. (D.I. 250 at 10).

75. The claims themselves do not reference "commercial use" and instead simply describe processes for obtaining a "pharmaceutical aqueous solution" by providing a solution comprising the 177Lu-Dotatate complex and then diluting the solution.

76. The specification does not specially define the term "pharmaceutical aqueous solution." Instead, it defines "aqueous solution" as "a solution of one or more solute in water" and states that "[t]he term 'pharmaceutical combination' as used herein means a product that results from the mixing or combining of more than one therapeutic agent." (JTX-0001.00017, 19).

77. The specification also describes embodiment 22b as "[t]he pharmaceutical aqueous solution according to any of the preceding embodiments, which is for commercial use." (JTX-0001.0006). That language would be redundant if all "pharmaceutical aqueous solutions" already required "for commercial use."

78. Moreover, as Dr. Dick pointed out, the use of the words "for commercial use" first appear in embodiment 22b. (Tr. 423:20-24 [Dick]). That means that embodiments 1 through 22a do not require "for commercial use" or that "over 99 percent of the embodiments of the patent do not require 'for commercial use.'" (*Id.*; Tr. 440:23-441:1 [Dick]).

79. Nothing in the prosecution histories of the Asserted Patents suggests that the claims are limited to products ready for commercial use.

E. Person of Ordinary Skill in the Art

80. Defendants' experts testified that the relevant person of ordinary skill in the art would "be skilled in pharmaceutical formulations, including methods of making them," and would "ideally have an advanced degree in pharmaceutical science or a related discipline," or alternatively "a lesser degree, but years of experience with pharmaceutical compositions, including the preparation and/or formulation of such compositions." (Tr. 310:18-311:6 [Nunn]; *see also* Tr. 410:4-13 [Dick]). Further, because manufacturing a radiopharmaceutical is "almost always a team

effort, [a POSA] would have to be able to interface with individuals having specialized knowledge outside their primary experience." (Tr. 311:3-6 [Nunn]; *see also* Tr. 410:14-16 [Dick]).

81. Plaintiffs' experts testified that the relevant personal of ordinary skill in the art comprises "a team of experts including radiochemists, individuals skilled in manufacturing radiopharmaceuticals for use as therapeutics, medical doctors, and individuals skilled in treating patients with radiopharmaceuticals. And the team would also work with people skilled in conducting clinical trials, analyzing the results of those trials and preparing submissions for regulatory approval." (Tr. 71:20-72:4 [Price]; *see also* Tr. 115:22-116:3 [Edwards]).

82. Neither party asserts that differences in the proposed constructions of a person of ordinary skill in the art are meaningful to any issue before the Court. This Court's conclusions do not change regardless of which party's definition is applied.

F. Infringement

83. ADACAP asserts that Lantheus's Product infringes claim 12 of the 276 Patent and claims 3 and 8 of the '003 Patent and that Curium's Product infringes claim 13 of the '276 Patent, claims 3 and 8 of the '003 Patent, claim 6 of the '063 Patent, and claims 3, 6, and 15 of the '732 Patent. Curium disputes infringement of all Asserted Claims. Lantheus disputes infringement of claim 12 of the '276 Patent but does not contest infringement of claims 3 and 8 of the '003 Patent. (D.I. 309, Ex. 1 ¶ 9).

84. Lantheus stipulated that Lantheus's Product meets all limitations of claims 3 and 8 of the '003 Patent. (D.I. 328 ¶ 9). Based on that stipulation, Lantheus's Product infringes claims 3 and 8 of the '003 Patent if those claims are not invalid.

85. Many of the claim elements of the Asserted Claims are not disputed, but Defendants still contest infringement on numerous bases. In this opinion, the Court addresses two of those arguments, namely:

(i) whether Lantheus' Product or Curium's Product meets the limitation of the Asserted Claims of the '276 Patent requiring that it "comprise[s] at least one stabilizer against radiolytic degradation that is different from the first stabilizer";

(ii) whether prosecution history estoppel precludes application of the doctrine of equivalents to the "total concentration" of stabilizer limitation in the Asserted Claims of the '276 Patent, the '003 Patent, the '063 Patent and the '732 Patent.

1. "Stabilizer ... That is Different from the First Stabilizer" In the Asserted Claims of the '276 Patent

86. As just noted (*supra* ¶ 83), ADACAP asserts that Lantheus's Product infringes claim 12 of the '276 Patent and that Curium's Product infringes claim 13 of the '276 Patent. Claims 12 and 13 ultimately depend on claim 1, which claims the disputed element: "the aqueous dilution solution comprises at least one stabilizer against radiolytic degradation that is different from the first stabilizer." (JTX-0001.0021).

87. Defendants assert that their respective products do not meet this element because each product uses just a "first stabilizer": ascorbic acid in Lantheus's Product and sodium ascorbate in Curium's Product. (D.I. 360 at 29-30).

88. ADACAP argues that diethylenetriaminepentaacetic acid ("DTPA"), which is added in both Lantheus's Product and Curium's Product, is a second stabilizer, different from the first stabilizer. (D.I. 347 at 32).

a. Lantheus's Product

89. Lantheus submitted ANDA No. 217060 to the FDA for approval to engage in the commercial manufacture, use, offer for sale, sale, and/or import of a generic version of ADACAP's Lutathera injection prior to the expiration of the '276 and '003 Patents. (D.I. 309, Ex. 1 ¶ 35).

90. Like Lutathera, Lantheus's Product is an injection for intravenous administration containing the active ingredient Lutetium Lu 177 dotatate. (*Id.*, Ex. 1-A ¶ 1).

91. Lantheus stipulated that Lantheus's Product meets all of the limitations of claim 12 of the '276 Patent other than the limitation requiring that it comprise at least one stabilizer against radiolytic degradation that is different from the first stabilizer. (D.I. 328 ¶ 8).

92. Stabilizers against radiolytic degradation reduce degradation by "react[ing] with [] free radical[s], donating a proton, neutralizing the radical[s,] and preserving the Lutetium Dotatate so it doesn't get degraded." (Tr. 458:6-12 [Dick]).

93. According to the specification, "the stabilizers used in accordance with the present inventions may be selected from gentisic acid (2,5-dihydroxybenzoic acid) or salts thereof, ascorbic acid (L-ascorbic acid, vitamin C) or salts thereof (e.g. sodium ascorbate), methionine, histidine, melatonin, ethanol, and Se-methionine. Preferred stabilizers are selected from gentisic acid or salts thereof and ascorbic acid or salts thereof." (JTX-0001.0005).

94. Lantheus's ANDA describes a manufacturing process wherein a reaction buffer containing 81 mg/mL of ascorbic acid is added to the precursor solution, as well as the peptide Dotatate. (*See, e.g.*, DTX-4644; DTX-4652.0003; Tr. 217:12-22 [Smyth]).

95. $^{177}LuCl_3$ is then added to the formulation, which is heated and mixed to create a complexation reaction that forms the ^{177}Lu-Dotatate active ingredient. (Tr. 219:6-14 [Smyth]; DTX-4652.0002; DTX-4644.0015; DTX-4645.0002).

96. Ascorbic acid is a well-known antioxidant and works as a radiolytic stabilizer. (Tr. 220:1-8, 235:8-11 [Smyth]).

97. Ascorbic acid is one of the preferred stabilizers listed in the Asserted Patents. (JTX-0001.0005).

98. Ascorbic acid is one of the most effective stabilizers against radiolytic degradation because it can quickly react with the free radicals, preventing them from reacting with other organic molecules and thereby neutralizing the radicals. (Tr. 220:1-8, 234:11-235:18, [Smyth]).

99. Ascorbic acid is effective at reacting with free radicals within ^{177}Lu-Dotatate solutions because it has a fast reaction rate and can donate two electrons and therefore react with two free radicals per molecule. (*Id.*).

100. Ascorbic acid is present within Lantheus's ANDA Product in a concentration of 2.8 mg/mL, or 0.28% w/v. (DTX- 4645.0002; Tr. 235:21-25, 250:11-13 [Smyth]).

101. The parties do not dispute that the ascorbic acid in Lantheus's product meets the "first stabilizer" element of Claim 12. (*See* D.I. 328 ¶ 8; D.I. 348 ¶ 339).

102. After the complexation reaction in Lantheus's manufacturing process referenced above (*see supra* ¶95), a dilution solution which contains 0.05 mg/mL of the DTPA is added. (DTX-4648.0003; DTX-4645.0002).

103. The amount of ascorbic acid present in Lantheus's Product is approximately 56 times more than the amount of DTPA. (*See* Tr. 101:22-102:14 [Price])

104. DTPA is a well-known chelating agent. (Tr. 222:20-223:1, 254:9-12 [Smyth]; *see also* JTX-0001.0005-06).

105. DTPA is not considered a stabilizer in the radiopharmaceutical field. (*See, e.g.*, Tr. 221:20-222:2 [Smyth]; Tr. 480:19-22 [Dick] ("No, it's commonly known in the radiochemical community that DTPA is a chelator, it is not a stabilizer against radiolytic degradation.")).

106. The Asserted Patents refer to DTPA as a "[s]equestering agent." (JTX-0001.0006, 19). The patents further state that DTPA is "preferably in an amount to result in a concentration of from 0.01 to 0.10 mg/mL (preferably about 0.05 mg/mL)." (JTX-0001.0005). Further, Example 1 from the patents shows that DTPA is added to the formulation as a "Sequestering agent" at a concentration of 0.05 mg/mL. (JTX-0001.0020). In addition, claim 14 of the '276 patent refers to "the solution provided in [claim 2] step (2.1)," which comprises "at least one stabilizer against radiolytic degradation," and states that the solution "further comprises diethylenetriamine-pentaacetic acid (DTPA) or a salt thereof." (JTX-0001.0021).

107. The presence of DTPA facilitates the excretion of unbound Lu-177. The unbound Lu-177 "wants to go to . . . lesser energy levels" and seeks out molecules to bind to, such as DTPA. (Tr. 239:10-240:9-14 [Dr. Smyth]). The DTPA will chelate (or bind) to the unbound Lu-177. (*Id.*). The DTPA+Lu- 177 compound is known as "free" Lutetium, which will not irradiate healthy tissue. (*See* DTX-4650.0013 (noting that the "free" Lutetium includes "chelates formed between unbound lutetium-177 and components of the drug product matrix (e.g., DTPA, ascorbic acid and others"))). This free Lutetium, once formed, is safely processed by a patient's kidneys and passed through urine. (Tr. 222:3-14 [Smyth]; *see also* DTX-4644.0039).

108. Lantheus's ANDA consistently states that DTPA acts as a chelating agent. (Tr. 221:20-222:2 [Smyth]; DTX-4645.0002; DTX-4644.0073; DTX-4644.0039; DTX-4650.0028).

109. Lantheus' characterization of DTPA as a chelator is consistent with how ADACAP characterized DTPA in Lutathera. (Tr. 98:21-25 [Price]; Tr. 232:18-233:4 [Smyth] ("ADACAP told FDA in their NDA that DTPA was a sequestering agent, trapping agent, and chelating agent, and they said that consistent in their submission to the FDA."); *see also* DTX.0029.0006; DTX.0048.0180).

110. Nevertheless, ADACAP asserts that DTPA acts as a stabilizer against radiolytic degradation that is different from the ascorbic acid in Lantheus's Product. (D.I. 347 at 32-33).

111. ADACAP relies on the testimony of its expert, Dr. Price, who opined that DTPA's molecular structure allows it to bind to free radicals, thus acting as a stabilizer. (Tr. 74:9-76:1 [Price]).

112. Lantheus's expert, Dr. Smyth, did not dispute that DTPA could, theoretically, interact with free radicals. (Tr. 247:9-15 [Smyth]).

113. The inclusion of ascorbic acid will affect how DTPA acts in a formulation. (Tr. 241:2-14 [Smyth]).

114. One of the inventors of the Asserted Patents, Dr. Lorenza Fugazza, testified there would need to be tests done to "conclude that in a specific formulation this component has a specific function." (Tr. 207:11-17 [Fugazza]).

115. Dr. Price, however, did not perform any tests to establish whether DTPA functioned as a stabilizer in Lantheus's Product and did not know what the reaction rate is for DTPA in Lantheus's Product. (Tr. 97:22-98:6; 104:13-17 [Price]).

116. Dr. Price, instead, relied on literature unrelated to radiopharmaceuticals, including articles by Bibler, Mezyk and Thomas, to support his opinions that DTPA acts as a stabilizer in Lantheus's Product. (Tr. 240:20-22; 241:15-242:9 [Smyth]; Tr. 88:12-20; 90:8-21 [Price]).

117. The Bibler article is titled "Gamma and Alpha Radiolysis of Aqueous Solutions of Diethylenetriaminepenta-acetic Acid" and relates to research performed in a nuclear weapons facility. (Tr. 241:15-21 [Smyth]; JPTX-1378.0001; *see also* JPTX-1378.0009 (noting that the research was performed "during the course of work under Contract AT(07-2)-1 with the U.S. Atomic Energy Commission")).

118. The Mezyk article is titled "Radiolytic stability of metal-complexed extraction ligands under aqueous acidic reprocessing conditions" and relates to nuclear waste sites for nuclear fuel. (Tr. 241:22-242:2 [Smyth]; JPTX-1383.0001 ("The partitioning of the long-lived α-emitters and the high-yield fission products from dissolved nuclear fuel is key for safe recycling of nuclear fuel and disposition of high-level waste.")).

119. The Thomas article is titled "Pulse Radiolysis of the Reactivity of Metal Complexes of DTPA/Diethylene Triamine Pentaacetic Acid / With OH Radicals in Aqueous Solutions" and relates to atomic research performed at the Bhabha Atomic Research Centre. (Tr. 241:22-242:2 [Smyth]; JPTX-1381.0001).

120. None of these articles addresses how DTPA reacts in a pharmaceutical formulation with ascorbic acid. (Tr. 240:23-241:8 [Smyth]).

121. Dr. Price's opinion that DTPA acts as a stabilizer is based on its ability to interact with free radicals such that it sacrifices itself chemically to protect organic molecules. (Tr. 96:19-24 [Price]).

122. As Lantheus's expert Dr. Smyth explained, however, just because a molecule can react with a free radical does not mean it actually does so in a given formulation. (*See* Tr. 252:22-253:15 [Smyth]). And it also does not mean that it is reacting with a free radical in a meaningful way that renders it a stabilizer. (Tr. 253:16-19; 254:5-8 [Smyth]; *see also* Tr. 481:9-15 [Dick]).

123. ADACAP has provided scant evidence that DTPA reacts with free radicals within Lantheus's ANDA Product at all, let alone in a meaningful way that renders it a stabilizer. (*See* Tr. 253:5-254:8 [Smyth]).

124. Lantheus's ANDA showed that the average concentration of DTPA in Lantheus's product decreased from 0.0493 mg/mL to 0.0467 mg/mL after 60 hours. (PTX-1886.0027; Tr. 81:3-5 [Price]).

125. Although Dr. Price testified that this small decrease of about 0.0026 mg/mL was "consistent with activity as a stabilizer," he did not conclude that this decrease was "statistically significant." (Tr. 85:23-86:12 [Price] ("Q: But you don't know whether that number, the five % loss, is statistically significant, do you? A: No."); Tr. 108:21-109:5 [Price] ("So, from the data they provide, they can't fairly say that this is significant.")).

126. And Dr. Price acknowledged that there could be reasons for the decrease, including DTPA's chelating function or "potentially something else." (Tr. 81:9-82:18 [Price]).

127. Lantheus's expert, Dr. Smyth, testified that the decrease was "not statistically significant" and that therefore "there is no decrease in DTPA over the shelf life of the product." (Tr. 234:1-2 [Smyth]).

128. Dr. Smyth further testified that, "even if there were a decrease in DTPA concentration, it would be relating to this chelating function," given that the measurements at issue only capture "free unchelated DTPA." (Tr. 234:3-5, 236:6-16 [Smyth]).

129. Overall, although it may be that DTPA could theoretically act as a stabilizer, there is no persuasive evidence that DTPA actually does act as a stabilizer against radiolytic degradation in Lantheus's Product.

130. Thus, ADACAP failed to prove that DTPA functions as a stabilizer in Lantheus's Product by a preponderance of evidence.

b. Curium's Product

131. Many of ADACAP's arguments that DTPA acts as a stabilizer – and Defendants' arguments to the contrary – apply equally to Lantheus's Product and Curium's Product. (*See* D.I. 348 at 67-75, 80-82; D.I. 359 ¶ 577 ("DTPA is not a stabilizer against radiolytic degradation in Curium's 505(b)(2) Product for the same reasons DTPA is not a stabilizer against radiolytic degradation in Lantheus's ANDA Product.")). So too, many of the Court's Findings of Fact with respect to Lantheus's Product are also relevant to Curium's Product. (*E.g.*, FF ¶¶ 92-93, 104-106, 114). The Court thus incorporates those Findings of Fact in this section.

132. Curium submitted a New Drug Application pursuant to Section 505(b)(2) of the Hatch-Waxman Act ("505(b)(2) Application") No. 218525 with the FDA for approval to engage in the commercial manufacture, use, offer for sale, sale, and/or import a proposed Lutetium Lu 177 dotatate injection product prior to the expiration of the '276, '003, '732, and '063 Patents. (D.I. 309, Ex. 1 ¶ 39).

133. Like Lutathera, Curium's Product is an injection for intravenous administration containing the active ingredient Lutetium Lu 177 dotatate. (*Id.*, Ex. 1-B ¶ 1).

134. Curium's product contains sodium ascorbate. (Tr. 122:11-17; 125:24-126:13 [Edwards]; PTX-5972 at 2).

135. Curium's 505(b)(2) Application states that "[s]odium ascorbate functions as both a radiostabilizer and a pH buffer in the final drug product." (PTX-5966.0087).

136. The specification of the Asserted Patents identifies sodium ascorbate as a stabilizer against radiolytic degradation. (JTX-0001.0005).

137. The parties do not dispute that the sodium ascorbate in Curium's Product meets the "first stabilizer" element of Claim 13. (D.I. 347 at 32).

138. Curium's Product contains 0.05 mg/mL of DTPA. (Tr. 480:3-9 [Dick]). This amount is 260 to 340 times less than the amount of sodium ascorbate in Curium's Product. (Tr. 480:7-9 [Dick]).

139. In its 505(b)(2) Application, Curium characterizes DTPA as a "chelator." (PTX-5982.0010).

140. Curium's 505(b)(2) Application states that "DTPA is known to complex metals and is included as an excipient [in] the formulation to chelate any possible free Lu-177. When injected, the DTPA chelates unbound Lu-177 and the radioactive complex formed is rapidly excreted to prevent accumulation of free (non-chelated) Lu-177 in the bone." (PTX-5982.00084).

141. Curium's characterization of DTPA as a chelator is consistent with how ADACAP characterized the function of DTPA in Lutathera. (*See supra* ¶ 109).

142. Nevertheless, ADACAP asserts that DTPA acts as a stabilizer against radiolytic degradation that is different from the sodium ascorbate in Curium's Product. (D.I. 347 at 32-33).

143. ADACAP relies on the testimony of its expert, Dr. Edwards, who agreed with Dr. Price that DTPA's molecular structure allows it to bind to free radicals, thus acting as a stabilizer. (Tr. 122:20-123:11 [Edwards]).

144. Like Dr. Price, Dr. Edwards did not perform any testing to establish whether DTPA functioned as a stabilizer in the conditions present in Curium's Product. (Tr. 480:16-18 [Dick] "Q. Did any of ADACAP's experts test whether DTPA acts as a stabilizer in Curium's product? A. No.").

145. Dr. Edwards, instead, relied on the same literature as Dr. Price relied: articles by Bibler, Mezyk, Thomas, to support his opinions that DTPA acts as a stabilizer in Lantheus's Product. (Tr. 122:20-123:11 [Edwards]).

146. Dr. Edwards also referenced an article by Michail titled "Scavenging of Free-Radical Metabolites of Aniline Xenobiotics and Drugs by Amino Acid Derivatives: Toxicological Implications of Radical-Transfer Reactions" which relates to a study investigating "a novel scavenging mechanism of arylamine free radicals by poly- and monoaminocarboxylates" under certain manufactured conditions. (Tr. 123:9-13; PTX-3951.0001).

147. As previously addressed (*supra* ¶¶ 117-120), none of these articles addressed how DTPA reacts in a pharmaceutical formulation with sodium ascorbate.

148. That is relevant because the inclusion of sodium ascorbate will affect how DTPA acts in a formulation. (Tr. 481:12-15 [Dick]).

149. Dr. Edwards opined that based on his review of Curium's data, "you see a substantial decrease in DTPA concentration of approximately fifty % over that three-day period in the presence of radiation indicating that DTPA is being destroyed." (Tr. 124:6-9 [Edwards]; PTX-5554.0012; PTX 6482).

150. But "the amount[s] of radioactivities in the samples were not sufficient to cause the drop in the amount of DTPA that Dr. Edwards says is due to radiolytic degradation." (Tr. 481:2-8 [Dick]).

151. Further, the sodium ascorbate in Curium's Product is 260 to 340 times more prevalent than DTPA (a significant excess). (Tr. 480:7-9 [Dick]).

152. Thus, "[e]ven if DTPA could react with a hydroxyl group in Curium's product, . . . [t]he amount of sodium ascorbate [and] ethanol is so much more that it is extremely likely that

sodium ascorbate or ethanol would neutralize any free radicals before DTPA would." (Tr. 481:9-15 [Dick]).

153. Overall, although ADACAP provides evidence that DTPA could theoretically act as a stabilizer, there is no persuasive evidence that DTPA actually acts as a stabilizer against radiolytic degradation in Curium's Product.

154. Thus, ADACAP failed to prove by a preponderance of the evidence that DTPA functions as a stabilizer in Curium's Product.

2. "Stabilizers . . . in a Total Concentration"

155. All Asserted Claims are subject to limits on the "total concentration" of "stabilizers" in the drug. (JTX-0001.0021; JTX-0006.0023; JTX-0007.0023; JTX-0008.0023).

156. The Asserted Claims in the '276 Patent depend from claim 1, which recites that "stabilizers are present in a total concentration of from 1.0 to 5.0 mg/mL." (JTX-0001.0021).

157. The Asserted Claims in the '003 Patent, the '732 Patent and the '063 Patent depend from claims that recite "stabilizer(s) against radiolytic degradation is/are present in a total concentration of 0.5 mg/mL to 10.0 mg/mL." (JTX-0006.0023; JTX-0007.0023; JTX-0008.0023).

158. All Asserted Claims thus limit the total stabilizer concentrations to either 1.0 to 5.0 mg/mL or 0.5 mg/mL to 10.0 mg/mL.

159. Curium's Product contains a total concentration of stabilizer of 13 to 17 mg/mL[6] and falls outside of the patented range. (Tr. 125:23-126:4 [Edwards]).

160. ADACAP argues that Curium's Product meets the "total concentration" of stabilizer limitation under the doctrine of equivalents. (D.I. 347 at 13).

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[6] If DTPA is included as a stabilizer, then Curium's Product contains a total stabilizer concentration of 13.04 to 17.06. (Tr. 125:23-126:4). This difference does not materially alter the Court's analysis of this issue.

161. Curium argues, among other things, that ADACAP is estopped from relying on the doctrine of equivalents for the "total concentration" of stabilizer limitation due to its claim amendments during patent prosecution. (D.I. 360 at 3).

a. The '276 Patent Prosecution History

162. On October 30, 2018, ADACAP filed the '261 Application, which ultimately issued as the '276 Patent. (JTX-0001.0001; JTX-0002).

163. The '261 Application initially claimed a process in which "the stabilizers are present in a total concentration of from ***0.2 to 20.0 mg/mL.***" (JTX-0002.0015) (emphasis added). This claim, had it been allowed, would have literally encompassed the total concentration of stabilizer (13 to 17 mg/mL) in Curium's Product. (Tr. 159:12-15 [Edwards]).

164. On February 12, 2019, the Patent Examiner rejected claims 1-21 under 35 U.S.C. § 103 "as being unpatentable over Chen et al. (US 2007/0269375A1) [("Chen")] in view of Maus et al. (*Int. J. Diagnost. Imaging* 2014, 1, 5-12) [("Maus")]." (JTX-0002.0130).

165. Among other things, the Patent Examiner explained that, in Chen, the "gentisic acid is used in a concentration 2-20 mg/ml and ascorbic acid is used in a concentration 10 to 100 mg/ml." (JTX-0002.0130).

166. The Patent Examiner noted that gentisic acid and ascorbic acid are both stabilizers. (JTX-0002.0130-131).

167. In the February 12, 2019 Office Action, the Patent Examiner also rejected claims 6-9 that depended from original claims 1 and 2 under "35 U.S.C. § 112(d) or pre-AIA 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends." (JTX-0002.0129).

168. On May 13, 2019, the applicant responded to the February 12, 2019 Office Action. (JTX-0002.0230-239). The applicant's amendment narrowed claim 1 to limit the total concentration of stabilizers as follows:

> the stabilizers are present in a total concentration of **from ~~0.2 to 20.0~~ 1.0 to 5.0 mg/mL**.

(JTX-0002.0236) (emphasis added).

169. In the argument submitted alongside the amendment, applicant explained, *inter alia*:

> In other words, Chen teaches a total concentration of stabilizers being about 32-33 mg/mL, at a volumetric radioactivity of 25mCi/mL ^{177}Lu, which is equivalent to about from **8.7 to 17.8 mg/mL** of total concentration of stabilizers at a volumetric radioactivity of **6.8-13.5 mCi/mL** ^{177}Lu. In comparison, the total concentration of the stabilizers recited in independent claim 1 is **much lower** than that of Chen (***1.0 to 5.0 mg/mL*** total concentration of stabilizers at a volumetric radioactivity of **6.8-13.5 mCi/mL** ^{177}Lu). Noticeably, Chen **teaches away** from using such low concentrations of stabilizers in the final radiopharmaceutical formulations disclosed thereof.

(JTX-0002.0232) (emphases in original).

170. Applicant also argued that Maus "refers to a noticeably higher total concentration of gentisic acid and ascorbic acid" and "[m]ore importantly, Maus also teaches away from using lower concentrations of gentisic acid and ascorbic acid." (*Id.*; *see also* JTX-0002.0233 (arguing that Maus "refers to a noticeably higher total concentration of gentisic acid and ascorbic acid (equivalent to 5-10 mg/mL at a volumetric radioactivity of 6.8-13.5 mCi/mL ^{177}Lu and up to 15.4 mg/mL gentisic acid or 17.6 mg/mL ascorbic acid sodium salt at a volumetric radioactivity of 13.5 mCi/mL ^{177}Lu).")).

171. Applicant continued that "in view of the unpredictable nature of stabilizers (e.g., their types, timing of adding them, and their amounts) taught by the primary reference, Chen, as

well as the teachings away from both Chen and Maus, a skilled artisan would not have reasonably expected that the low total concentration of stabilizers recited in claim 1 would sufficiently stabilize the pharmaceutical aqueous solution obtained via the claimed process. . . . Accordingly, the claimed process of making such pharmaceutical aqueous solution recited in claim 1 is nonobvious over Chen and Maus." (JTX-0002.0232)

172. In response to the § 112 argument regarding claims 6-9, applicant did not reference its claim amendment as a ground to overcome the rejection. Instead, it stated:

> Applicant would like to point out that the stabilizers' concentration in claim 1 is that in the obtained pharmaceutical aqueous solution after a dilution step while the concentrations in claims 6-9 are those of stabilizer(s) present during the complex formation and before a dilution step. Applicant submits that claims 6-9, each of which depends from claim 1 indirectly, further limit claim 1 by providing additional features for various steps of the claimed process. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. 112(d) be withdrawn.

(JTX-0002.230).

173. The Patent Examiner then withdrew the "[t]he rejection of claims 1-21 under 35 U.S.C. 103 as being unpatentable over Chen . . . in view of Maus" and the § 112 rejection to claims 6-9. (JTX-0002.0256).

174. The Examiner also issued a new obviousness rejection, asserting that the claims were "unpatentable over de Blois et al. . . . in view of Singh et al. . . . and RCM meeting . . . and in further view of Maus et al. . . . and Chen et al. (US 2007/0269375A1)." (JTX-0002.0259).

175. In particular, the Examiner stated that de Blois disclosed each limitation of pending claim 1, including ascorbic acid and gentisic acid, with a total stabilizer concentration of from 1.0 to 5.0 mg/mL, except "de Blois et al. does not disclose 250-500 MBq/mL ... of radionuclide."

(JTX-0002.260). The Examiner pointed to Singh et al. as disclosing that limitation and rendering claim 1 obvious. (JTX-0002.260-61).

176. On June 6, 2019, applicant responded. It argued, among other things, that "both Maus and Chen **teach away** from using the low concentration of stabilizers (i.e., 1.0-5.0 mg/mL) for high volumetric radioactivity (i.e., 250-500 MBq/mL) recited in claim 1." (JTX-0002.0435 (emphasis in original)).

177. "Curium's total stabilizer concentration range is within the scope of a range that ADACAP told the patent examiner taught away from its much lower claimed total stabilizer concentration range after the amendment." (Tr. 160:17-21 [Edwards]).

178. Applicant argued "independent claim 1 is also patentable over de Blois in view of Singh, RCM, Maus and Chen for unexpected stability of the pharmaceutical solution produced by the claimed method, even when the obtained solution has the low total concentration of stabilizers recited in claim 1." (JTX-0002.0436).

179. The Examiner initially maintained the objection (JTX-0002.0462) but ultimately allowed the claims following further amendments to the amounts of ethanol present. (JTX-0002.0493).

180. ADACAP now argues that its amendment to claim 1 addressed a "purely formal claim dependency issue" that was "non-substantive" and "cosmetic." (D.I. 347 at 27; D.I. 365 at 15-16). According to ADACAP, the amendment was a response to the Patent Examiner's determination in the February 12, 2019 rejection that "Claims 6-9 are rejected under 35 U.S.C. 112(d) or pre-AIA 35 U.S.C. 112, 4th paragraph, as being of improper dependent form." (JTX-0002.0129).

181. It not credible that ADACAP narrowed its claim to give up more than 75 percent of its claimed total stabilizer range to address "non-substantive" and "cosmetic" claim-dependency issues.

182. ADACAP's litigation narrative is also contradicted by countervailing facts, including that the Patent Examiner rejected claims 1-21 as "unpatentable" over prior art; that the Patent Examiner explained prior art taught high total stabilizer concentrations; that applicant justified its amendment to claim 1 as encompassing lower concentrations of stabilizers than prior art; that applicant did not argue the amendment in trying to overcome the § 112 rejection; and that the Patent Examiner then withdrew the patentability rejection.

183. ADACAP's statements to the Patent Examiner that "it is not conceded" that the amendment was "necessary to distinguish the art of record or to satisfy the requirements of 35 U.S.C. § 112" are unavailing. (JTX-0003.00143-44). These are simply self-serving assertions and do not overcome the facts stated in the previous paragraph.

184. ADACAP argues that, after the '276 Patent was issued, the Patent Office permitted broader stabilizer ranges in later-issued Asserted Patents. (D.I. 347 at 8, 24). The Patent Office, however, never allowed original claim 1 in later patents.

185. The claims of the'003 Patent, the '063 Patent and the '732 Patent that ADACAP rely on include broader total concentration ranges of stabilizers than the '276 Patent; but none of those ranges is broad enough to include Curium's Product. (*See supra* ¶¶ 158-159).

186. The claims of U.S. Patent No. 12,415,003 ("the '5003 Patent") do include a total concentration of stabilizer that would cover the Curium product. Those claims also contain additional limitations that narrow the claims, and that patent has not been asserted against Curium in this case.

187. All of the later broader claims that Curium relies on include additional limitations that narrowed those claims in different ways. For example, claim 1 of the '276 patent does not limit the activity or volume of the pharmaceutical aqueous solution, but claim 1 of the '003 patent requires that "the activity of the pharmaceutical aqueous solution is 7.4 GBq ±10%" and "the volume of the pharmaceutical aqueous solution is 10 mL to 50 mL." (*See* JTX-0001.0021; JTX-0008.0023).

b. The '003, '632 and '732 Patent Prosecution Histories

188. In 2024, after the '276 Patent issued, ADACAP began prosecuting related applications that ultimately issued as the '003, '063, and '732 Patents. (JTX-0006.0001; JTX-0007.0001; JTX-0008.0001).

189. Each of those applications initially recited, in claim 1, that "stabilizer(s) against radiolytic degradation is/are present in a total concentration of ***0.2 mg/mL to 20.0 mg/mL***." (JTX-0003.0059; JTX-0004.0101; JTX-0005.0060 (emphasis added)). These claims, had they been allowed, would have literally encompassed the total stabilizer range of 13 to 17 in Curium's Product. (Tr. 159:12-15 [Edwards]).

190. Prior to any action on each of the applications, applicant initiated an interview with the Patent Examiner. The interview took place on August 21, 2024. (JTX-0003.0122; JTX-0004.0122; JTX-0005.0122).

191. The Examiner summarized the interviews in Applicant-Initiated Interview Summaries in virtually identical language in each of the applications:

> The Examiner discussed the references used in the previously allowed applications that apply to the instant claims: deBlois (Appl. Radiat. Isotop 2014), Singh (Ind J. Nucl. Med. 2011), Maus (int J. Diagnost. Imaging 2014) and RCM meeting 2012.
>
> The Examiner discussed that the reasons for allowance of the previously allowed parent and/or related applications was due to the

> combination of ***the low total concentration of*** stabilizers present in the pharmaceutical aqueous solution, less than 1% of EtOH in the pharmaceutical aqueous solution and/or an RCP that is maintained at greater than equal to 95% for at least 72 h when stored at 25 degrees C.

(JTX-0003.0122; JTX-0004.0122; JTX-0005.0122) (emphasis added).

192. Thereafter, on September 10, 2024, applicant submitted amendments to each of the three applications that narrowed the total stabilizer concentration range ***from "0.2 mg/mL to 20.0 mg/mL" to "0.5 mg/mL to 10.0 mg/mL***." (JTX-0003.0138; JTX-0004.0138; JTX-0005.0134; *see also* Tr. 162:14-163:1 [Edwards]) (emphasis added).

193. Applicant also amended the claims to address the amount of ethyl alcohol, i.e., adding the language "the pharmaceutical aqueous solution comprises less than 1% ethanol."[7] (*Id.*).

194. Thus, less than three weeks after the Examiner explained that she had previously allowed related applications in part because they contained lower total concentrations of stabilizers, applicant narrowed the total claimed stabilizer ranges by more than 50 percent and limited the amount of ethanol to less than 1%. (*Id.*).

195. ADACAP argues that these amendments were unrelated to patentability, reiterating the arguments concerning the '276 Patent and noting that the '003, '063, and '732 Patents recite broader total stabilizer ranges than the '276 Patent. (D.I. 347 at 23-27). Yet, as previously noted, these later-claimed ranges still fall below ADACAP's initially-claimed range.

196. In sum, ADACAP amended its claims to reduce the total concentration of stabilizer claimed from 0.2 to 20.0 mg/mL to 0.5 to 10.0 mg/mL to address the Patent Examiner's comments about the patentability of higher stabilizer range in light of various prior art references.

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[7] Defendants argue that this amendment also estops ADACAP from asserting that the ethyl alcohol limitation in the claims is met by equivalents. (D.I. 360 at 26).

197. In doing so, ADACAP gave up the range of total concentration of stabilizers that would have literally covered Curium's Product. ADACAP is now precluded from invoking the doctrine of equivalents to broaden its claims now to cover Curium's Product.

G. Validity

198. As with infringement, Defendants raised numerous bases on which they assert that the Asserted Claims are invalid. In this opinion, the Court addresses Defendants' assertion that all Asserted Claims are invalid based on application of the on-sale bar.

199. For purposes of the on-sale bar, the parties agree that the priority date for all Asserted Patents is July 25, 2018, and the critical date for all the Asserted Patents is July 25, 2017. (D.I. 331 ¶ 1).

a. Pre-Critical Date Lutathera

200. ADACAP stipulates that Lutathera made and sold before the critical date met all but two of the limitations of the Asserted Claims. (D.I. 331 ¶ 2). Specifically, ADACAP asserts that pre-critical date Lutathera failed to meet the limitations: "[a] method of manufacturing a pharmaceutical aqueous solution" and "pharmaceutical aqueous solution" under its proposed construction of those limitations, i.e., "a drug product suitable for commercial use and approvable by regulators." (*Id.*; D.I. 357 at 18-19).

201. The full stipulation regarding the pre-critical date product provides as follows:

> The lutetium Lu 177 dotatate product made by ADACAP and (i) cited by ADACAP as a pivotal batch or a validation batch in its original or resubmitted New Drug Application for Lutathera, (ii) provided to others in clinical trials, and/or (iii) provided to others on a compassionate use or named-patient basis before the critical date, including through the U.K. Specials program and including at least batches LT141124A-03, LT150713A-03, LT150713A-06, LT150720A-06, LT160411A-03, LT160502A-03, LT160517A-03, LT160606A-03, LT160822A03, LT160912A-03, LT161010A-03, and LT170426A-03, and doses from them, met all limitations of Claims 3 and 8 of the '003 Patent, Claim 15 of the '732 Patent, and was made by a process that met all limitations of Claims 12 and 13 of the '276 Patent, Claims 3 and 6 of the '732 Patent, and Claim 6 of the '063 Patent, as currently construed by the Court, except that ADACAP contests that the "A method of manufacturing

> a pharmaceutical aqueous solution" and "pharmaceutical aqueous solution" limitations were met under its proposed constructions for those terms. The parties' disputes on this issue will be presented at trial.

(D.I. 328 ¶ 2).

202. As explained below, the Court rejects ADACAP's construction of "pharmaceutical aqueous solution" in the disputed terms and adopts the ordinary meaning construction offered by Defendants. (*Infra* Section III.B.1). As a result, Lutathera sold by ADACAP before the critical date met all the limitations of the Asserted Claims.

203. Moreover, Lutathera worked for its intended purpose by November 24, 2014. (Tr. 441:3-441:15 [Dick]). Dr. Dick analyzed certain batches from November 14, 2014, which he determined "were able to obtain regulatory approval as evidenced by the fact that those batches were included in the NDA that did obtain regulatory approval." (*Id.*).

204. The "formulation" of Lutathera remained the same since at least November 2014, and ADACAP did not "change its manufacturing process in any way material to the patent claims" since that time. (Tr. 441:19-442:1 [Dick]).

205. Although ADACAP's expert, Dr. Edwards, testified that the "[t]he purpose of the invention was to develop an industrialized manufacturing process that would allow Lutathera to be made at a central location in high purity and high stability, and be distributed to remotely located end users," and he asserted that the subject matter of the claims was not shown to work for its intended purpose before the critical date (Tr. 816:13-20 [Edwards]), he acknowledged that ADACAP was manufacturing Lutathera "at commercial scale" and sending Lutathera to "remote locations" by the end of 2012.

> Q. And you understand that at least by the end of 2012, ADACAP was manufacturing batches of Lutathera at commercial scale in a central manufacturing facility, correct?
>
> A. Yes.

Q. And ADACAP, by the end of 2012 at least, was shipping those batches to remote end users such as doctors and hospitals throughout the EU and the UK, correct?

A. I don't know the exact countries, but they were shipping them to remote locations.

(Tr. 841:17-25 [Edwards]).

206. SEC filings indicate that ADACAP initially did not intend to patent Lutathera. On October 4, 2016, ADACAP publicly declared that Lutathera was not and would never be covered by any patents. (*See* DTX-4987.0068 ("Our lead radiotherapeutic product candidate, Lutathera, is not covered by any patents and will not be covered by any patents in the time before, during, and/or after the period of its commercialization.")).

207. Two days later, on October 6, 2016, ADACAP repeated this assertion in another SEC filing. (DTX-0837.0036 ("Our lead radiotherapeutic product candidate, Lutathera, is not covered by any patents and will not be covered by any patents in the time before, during, and/or after the period of its commercialization.")).

208. Novartis acquired ADACAP in January 2018. (See Tr. 616:12-14 [Dr. Sullivan]; 855:24-856:3 [Edwards]; DTX-0698).

209. The "initial idea to file the family of patents that issued as the patents-in-suit" did not come from ADACAP; it came from the Novartis R&D IP group in 2018. (*See* Tr. 392:22-393:6 [Witkowski]; Tr. 408:8-13 [Dick]).

b. Expanded Access Programs

210. Beginning in 2012, ADACAP provided thousands of doses of Lutathera in exchange for payment in European and UK "expanded access programs." (*See* Tr. 407:23-408:2 [Dick]; Tr. 604:25-605:13 [Sullivan]; *see generally* DTX-0740).

211. The term "expanded access program" is a "high level term" that refers to both "compassionate use and named patient programs." (Tr. 531:21-25 [Litwak]). Compassionate use

programs permit "a group of patients to have access to a drug prior to health authority approval when there is an unmet need." (Tr. 532:1-4 [Litwak]). Named patient programs "follow a different regulatory pathway and are for individual patients." (Tr. 532:6-7 [Litwak]).

212. Expanded access programs generally "make drugs available to patients before the drug is approved" and will sometimes be used in a "life threatening situation" where "there is no other treatment available." (Tr. 526:4-8 [Nader]).

213. Companies do not generally start an expanded access program until they have "well-known safety and efficacy data because if an adverse [safety] event occurred" during an expanded access program, "there is no way to understand really what the root cause of the adverse event is, and it may create a safety signal that ultimately derails your clinical trial program or the health authority approval." (Tr. 533:2-14 [Litwak]).

214. Countries do not require pharmaceutical companies to provide drugs under expanded access programs; instead they are voluntary programs entered into by drug providers. (Tr. 679:18-21 [Cropp]).

215. Orders through expanded access programs are generally initiated by the physician. (Tr. 679:12-17 [Cropp]).

216. Companies are allowed to charge money for drugs supplied under expanded access programs in Europe. (Tr. 689:9-11 [Cropp]). The price a company can charge for a particular product varies depending on the country, resulting from negotiations between pharmaceutical companies and health authorities. (Tr. 689:12-16 [Cropp], Tr. 746:15-25 [Malackowski]).

217. In some countries companies can charge only for "cost of production and the shipping"; in other countries, "it will be a little more inclusive, such as . . . administrative" costs; and the pricing will ultimately "vary from country to country." (Tr. 695:18-23 [Cropp]).

218. Defendants' expert, Dr. Bravery, testified she was not aware of any pre-critical date restrictions on drug prices in the United Kingdom's expanded access program (which is called the "specials" program). (Tr. 568:20-569:4 [Bravery]). Another expert, Ms. Dennis, testified that United Kingdom pricing depended on the amount that a regional committee determined it could afford, a negotiation, and timing – leading Ms. Dennis to describe the process as a "bit of [a] pricing lottery." (Tr. 651:10-652:11 [Dennis]).

219. Thus, although some European regulations may limit expanded access sales to "cost recovery" in an abstract sense (Tr. 556:18-24 [Litwak]), in practice prices will vary among European countries, and sellers may be allowed to recover more than their true costs.

c. Commercialization

220. Prior to the critical date, ADACAP sold thousands of doses of Lutathera that went to nearly two thousand patients in ten European[8] countries: Austria, France, Estonia, Finland, Greece, Spain, Portugal, Denmark, Switzerland, and the United Kingdom. (*See* DTX-740 (tab "Hosp. & Distrib."); Tr. 605:2-13, Tr. 612:9-13 [Sullivan]).

221. Lutathera was sold at prices ranging from approximately €221 to €16,000, plus transportation costs. (Tr. 605:21-606:24 [Sullivan]).

222. The transactions generally took the form of sales from ADACAP to distributors followed by sales from distributors to hospitals. (*See* DTX-0740, tab "Hosp. & Dist.," column H).

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[8] In June 2015, ADACAP entered into an agreement with Fujifilm RI Pharma Co., Ltd ("the Fujifilm Agreement"). (DTX-0075). The Fujifilm Agreement was characterized as an "exclusive distribution and license agreement for Lutathera in Japan." (DTX-4987 at 182). Defendants argue that this also constitutes a commercial offer for sale that triggers the on-sale bar. But because this Court resolves the on-sale bar issue with respect to the European sales, it does not reach the Fujifilm Agreement.

223. For instance, from 2014 to 2016 ADACAP sold Lutathera to its UK subsidiary and distributor in the United Kingdom – Imaging Equipment Limited ("IEL") – for £4,500 plus transportation costs. (Tr. 606:9-20; 609:8-12 [Sullivan]; *see* DTX-0079.0032). IEL would then sell Lutathera to the customer (i.e., the hospital) for £6,000 plus transportation costs. (*See id.*).

224. Before the critical date, ADACAP also sold Lutathera for €8,000 to €9,000 per dose in Finland, €9,500 per dose in Denmark, €14,000 per dose in Spain, €6,000 to €16,000 per dose in France, €4,500 to €9,000 per dose in Austria, and €5,600 to €12,800 per dose in Switzerland. (Tr. 609:13-15; Tr. 611:3-5 [Sullivan]; DTX-1008 at 105).

225. By the critical date, ADACAP had sold more than £10 million of Lutathera in the United Kingdom. (Tr. 607:3-5 [Sullivan]).

226. The European sales continued in significant numbers from the end of 2012 through the critical date of July 25, 2017. (DTX-1008.0107-145).

227. In SEC filings, ADACAP referred to its provision of Lutathera under expanded use programs as "sales." (DTX-4987.0148-49).

228. For instance, ADACAP reported to the SEC that "[s]ales increased 26.8% or €18.7 million, from €69.9 million for the year ended December 31, 2014 to €88.6 million for the year ended December 2015," with €7.8 million of the increased sales resulting in part "from increased sales of Lutathera on both a named patient and compassionate use basis." (*Id.*).

229. Another SEC filing explained that ADACAP "realize[s] sales from our PET and SPECT products, enriched water and product candidates, including Lutathera. . . . Sales are recognized when the following conditions are met: there is an agreement between the parties; the goods have been delivered or the services rendered; the price is fixed or can be reliably measured; and it is probable that future economic benefits from the transaction will flow to us." (DTX-

0837.0070). In the same SEC filing, ADACAP reported "increased sales of Lutathera of €4.5 million on both named patient and compassionate use basis" for the six months ending on June 30, 2016, compared to the six months ending on June 30, 2015." (DTX-0837.0076).

230. Internal ADACAP documents demonstrate that that ADACAP received financial benefits from expanded use sales of Lutathera.

231. An ADACAP PowerPoint presentation in the fourth quarter of 2016 for ADACAP's board reported that Lutathera is "by far the most profitable" product in the context of the company's "sales." (Tr. 607:6-16 [Sullivan]; DTX-0730.0012). Another ADACAP presentation for the board, which focused on the first quarter of 2017, discussed "Lutathera sales in France" and, in the context of "[g]ross profit margin," referred to "high margin Lutathera." (Tr. 608:15-609:2 [Sullivan]; DTX-0738.0003).

232. Other internal ADACAP documents also evidence sales. These include the spreadsheet tracking all of the doses that ADACAP sold under its compassionate use and named-patient program (DTX-0740; DTX-0046); order forms (DTX-0941, DTX-0450.0097-100, DTX-0454, DTX-0468, DTX-0489, and DTX-0513); release records (DTX-0938.0251, DTX-0450.0105-106, DTX-0459, DTX-0471), and purchase orders (DTX-0947, DTX-0154, DTX-0115, DTX-0472, DTX-0834).

233. "[S]ubstantial profits . . . were earned on the gross margin basis and marginal profit basis" from pre-critical date sales of Lutathera." (Tr. 617:7-11 [Sullivan]).

234. Dr. Sullivan performed an analysis of Lutathera's marginal cost against the price at which Lutathera was sold prior to the critical date. He found that the marginal cost was between 1,440 and 2,561 Euros per dose. (Tr. 615:14-15 [Sullivan]). He then explained that "ADACAP was selling Lutathera prior to the critical date were much higher than the marginal costs" – as

referenced above, at prices between €4,000 to €16,000 – leading to "gross profit margins of roughly seventy percent." (Tr. 615:18-22 [Sullivan]).

235. Although ADACAP's expert, Mr. Malackowski, testified that the "marginal cost" approach left out key costs – including regulatory expenses, legal expenses, operating expenses of the company, research and development, executive compensation, and wasted doses (751:22-752:6, 777:2-778:5 [Malackowski]) – these costs apply across the company, e.g., all legal and regulatory costs incurred by the company, regardless of whether such costs were related to ADACAP's pre-critical date sales of Lutathera. (Tr. 613:12-16, Tr. 623:14-16, Tr. 624:10-12 [Sullivan]).

236. The Court found Dr. Sullivan's marginal cost analysis to be credible and persuasive. It shows that ADACAP received "additional financial benefits for each individual sale" of Lutathera that exceeded marginal costs prior to the critical date. (Tr. 613:17-23 [Sullivan]). In other words, "there is a positive contribution being made to ADACAP for those additional sales." (Tr. 613:7-10 [Sullivan]).

237. Further, Defendants' expert, Dr. Litwak, testified that "degree of commercial exploitation and contacts made with potential customers" through the European expanded access programs provided ADACAP with "significant commercial benefits." (Tr. 541:11-13 [Litwak]). She explained that "[a]ssuming they can minimize the risks, there are tremendous commercial benefits actually to having a compassionate use program. Having the ability to engage with physicians in advance of the post marketing approval. Having the opportunity to educate and have institutions educated on how to use the drug. Awareness of the brand is another commercial benefit. And of course, in this case, sales." (Tr. 533:17-24 [Litwak]).

238. Th Court ultimately agrees with Defendants that ADACAP sought and obtained financial benefits from these sales.

d. Experimentation

239. ADACAP argues that its expanded use sales were "experimental" because they were necessary to "develop and validate the manufacturing process." (D.I. 357 at 8, 24; Tr. 815:4-9 [Edwards] ("development in my opinion is one large experiment, so I view it as each small individual experiment as part of that large experiment. . . . [ADACAP was] collecting all this information in order to utilize that information and determine whether their process was performing as expected.")).

240. ADACAP relies on an Excel spreadsheet in which it tracked various kinds of information related to expanded use doses. (*see generally* DTX-0740).

241. The Excel spreadsheet was simply "routine tracking of normal manufacturing data," and it is standard practice to "chart all of the manufacturing and quality control parameters and look for trends that might indicate issues." (Tr. 444:6-24 [Dick]).

242. Indeed, Dr. Edwards agreed that the same data is collected for "true commercial sales":

> Q. In fact, ADACAP was tracking exactly the same information after approval when it was manufacturing Lutathera for what everyone in this courtroom would agree were true commercial sales, right?
>
> A. I believe so.
>
> . . .
>
> Q. So all of the information that you're testifying here as part of the one big experiment was actually being tracked by ADACAP as part of its standard manufacturing processes, right?
>
> A. After approval. Just because you're collecting data during development doesn't mean you stop collecting it after you get approval.

(Tr. 852:11-853:13 [Edwards]).

243. ADACAP did not "identify any documentation of design plans or protocols for any experiments relating to manufacturing Lutathera for the expanded access programs." (Tr. 445:2-6 [Dick]). Nor did it identify "[a]ny reports of experiments completed," "[a]ny evidence that any doses were manufactured for experiments" or "any evidence that ADACAP conducted any manufacturing experiments" at all. (Tr. 445:7-14 [Dick]).

244. And ADACAP did not track data in a manner that suggests experimentation.

245. ADACAP submitted "204 produced compassionate use doses" to regulatory authorities as part of obtaining regulatory approval. (D.I. 357 at 19-20). Those 204 doses were all manufactured by November 16, 2015, meaning that thousands of compassionate use doses produced after this date (yet before the critical date) were not submitted to regulatory authorities to obtain approval. (*See* D.I. 358 ¶ 117).

246. All 204 doses were used for the ADACAP's NETTER-1 trial and thus have no bearing on the experimental nature of sales that took place after the conclusion of the NETTER-1 trial. (*See* DTX-0108.2529).

247. ADACAP also offers some evidence that it changed characteristics of Lutathera in response to what it learned from expanded access sales. (D.I. 357 at 7-8, 19). But by ADACAP's own admission, the Lutathera sold in the expanded access programs already met all limitations[9] of the Asserted Claims. (D.I. 331 ¶ 2).

248. ADACAP's expert, Dr. Edwards, also confirmed that all the data reflected in the patents is from 2014:

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[9] ADACAP's only argument that expanded access Lutathera did not satisfy all limitations of the Asserted Claims is based on a construction that this Court rejects in Section III.B.1.

Q. None of the results or learning from any of this experimentation you're pointing to is reflected in the patents, all the data in the patents is from 2014.

A. All the data is from 2014, yes.

(Tr. 851:10-13 [Edwards]).

249. On this record, this Court cannot conclude that the primary purpose of ADACAP's expanded use sales of Lutathera was experimentation.

e. The NETTER-1 Trial

250. The NETTER-1 trial was a Phase III clinical trial evaluating Lutathera beginning in July 2012 and meeting its "primary endpoint" by September 16, 2015. (*See* DTX-0656.0001; Tr. 407:19-22, Tr. 443:10-17 [Dick]).

251. The NETTER-1 trial provided "real world data on the manufacturing and distribut[ion] of Lutathera to forty-one centers across eight countries." (Tr. 446:10-15 [Dick]).

252. The NETTER-1 trial "evaluated the efficacy and safety of lutetium-177 (177Lu)-Dotatate in patients with advanced, progressive, somatostatin-receptor-positive midgut neuroendocrine tumors." (PTX-1902.0001).

253. The NETTER-1 trial was overseen by a Data Safety Monitoring Board, which is a "group of independent individuals, physicians, biostatistics experts, and patient advocates that review interim data in clinical trials regarding efficacy and toxicity and make recommendations on whether the trial should continue, change, or be canceled." (Tr. 438:13-18 [Dick]).

254. On October 16, 2014, the Data Safety Monitoring Board for the NETTER-1 clinical trial unanimously recommended that the study be halted because it would be unethical to continue providing an inferior treatment to patients in the control group. (DTX-0934.0002). The Board explained that given "overwhelming evidence of the benefit of ^{177}Lu-DOTA0-Tyr3-Octreotate

treatment on Progression Free Survival (PFS) in this trial, no new patients should be randomized into the study." (*Id.*).

255. The "Data Safety Monitoring Board letter shows that people believed that Lutathera worked for its intended purpose and, in fact, was better than the treatments that were on the market at that time." (Tr. 440:8-11 [Dick]).

256. Indeed, Maurizio Mariani, one of the named inventors on the Asserted Patents, and others pointed to the Data Safety Monitoring Board letter "as the single greatest achievement or moment in their long experience with Lutathera®'s development" and explained that the letter "gave credence to their long-standing belief in the potential for Lutathera®." (DTX-0710.0008).

257. Nevertheless, ADACAP continued the study based on the belief that "more statistical data would be needed to justify an application for registration," which was "subsequently confirmed by discussions with regulatory agencies." (*Id.*). The FDA and European Medicines Agency ("EMA") both suggested that ADACAP should complete the trial for more robust data. (DTX-0934.0008-11).

258. In a September 16, 2015 press release, ADACAP announced that the "pivotal Phase 3 NETTER-1 clinical study investigating the treatment of Lutathera (177-Lu-Dotatate) . . . met its primary endpoint, demonstrating a statistically significant and clinical meaningful increase in progression-free survival." (*See* DTX-0656.0001; Tr. 443:10-12 [Dick]). That same day, named-inventor Giovanni Tesoriere was congratulated in an email regarding the press release. (*See* DTX-4562; DTX-4563; Tr. 862:3-22 [Edwards]).

f. <u>ADACAP's NDA</u>

259. ADACAP filed a New Drug Application ("the NDA") for Lutathera with the FDA on March 31, 2016 – more than a year before the critical date. (DTX-0108.0001).

260. On July 24, 2017, the day before the critical date, ADACAP submitted a revised version of the NDA ("the Revised NDA"), which was ultimately approved by the FDA. (DTX-0434). The Revised NDA adjusted formatting errors in the initial NDA but did not amend anything material to the drug product or the Asserted Claims. (Tr. 435:10-23 [Dick]; Tr. 864:21-865:1 [Edwards]).

261. Defendant's expert, Dr. Dick, testified that an NDA is "the single best source of information if you want to know how to make a drug product." (Tr. 434:25-435:3 [Dick]).

262. ADACAP's NDA discloses all elements of the Asserted Claims in "copious detail," provides a "complete roadmap on how to manufacture and use Lutathera," and contains "substantially more information . . . than there is in the examples listed in the patents." (Tr. 429:24-430:8, 433:9-10 [Dick]).

263. Dr. Dick engaged with the factors from *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) and determined that the NDA "very much was an enabling disclosure for a person of ordinary skill in the art." (Tr. 433:16-434:24 [Dick]).

264. Dr. Dick further testified:

> So the first factor is quantity of experimentation necessary. There would be no experimentation necessary. The NDA gives you the complete instructions on how to make and use Lutathera, which had already been very well developed at the time. In terms of the amount of direction or guidance, the NDA has thousands of pages that would direct you on how to make and use Lutathera. Working examples, there are multiple working examples of actual batches included in there to show you the results that you expect. The nature of the invention, Lutathera is a very straightforward manufacturing process for a drug that's identical to the Erasmus formulation. Nearly identical, I should say, to the Erasmus formulation. So this enables the nature of the invention. State of prior art. People had been using Lutathera for over a decade and published results on it, so there was significant prior art. Relative skill of those in the art. A POSA would have had all of those literature publications and would have the radiochemistry skill to implement what was in the NDA.

> And in terms of predictability or unpredictability of the art, Lutathera was very predictable at that time through the Erasmus data, through the publications that had been put out there. And by its nature, the NDA is a very predictable document because you have already developed and validated all of your manufacturing, as well as performed at least a Phase 3 clinical trial. So taking all of these into consideration, it was my view that this very much was an enabling disclosure for a person of ordinary skill in the art.

(Tr. 433:16434:24 [Dick]).

265. The NDA also contained stability studies for "twelve different batches" and "protocols on how to perform those stability studies, which are not provided in the patent." (*See* Tr. 431:20-432:7 [Dick]).

266. Curium's expert, Dr. Edwards, agreed that the Lutathera NDA "definitely" contains "much more information on Lutathera and how to manufacture it than what's presented in the specification of the asserted patents" and that it contains "extensive data on batches of Lutathera beyond what's presented in examples 1 through 3" of the patents. (Tr. 859:6-22 [Edwards]).

267. Dr. Edwards further agreed that the specification for the Asserted Patents is "an enabling disclosure for all the claims," but could not "identify any information . . . that's present in the specifications of the asserted patents that's not present in the Lutathera NDA." (Tr. 859:20-860:2 [Edwards]).

268. Dr. Edwards' basis for disagreeing that the NDA constitutes an enabling disclosure is that "the commercial use definition requires that the drug is able to obtain regulatory approval" and filing "[t]he NDA is just the start of that review." (Tr. 826:24-827:10 [Edwards]; *see also* Tr. 788:18-22 [Edwards]).

269. In light of the Court's rejection of ADACAP's proposed construction of the aqueous solution terms, the Court finds that the NDA disclosed, in detail, a drug product that met all elements of the Asserted Claims and constitutes an enabling disclosure.

II. LEGAL STANDARD

A. Infringement

A patent is infringed when a person "without authority makes, uses, offers to sell, or sells any patented invention, within the United States . . . during the term of the patent." 35 U.S.C. § 271(a). "The patentee bears the burden of proving infringement by a preponderance of the evidence." *Laitram Corp. v. Rexnord, Inc.*, 939 F.2d 1533, 1535 (Fed. Cir. 1991). Courts employ a two-step analysis in analyzing infringement. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd,* 517 U.S. 370 (1996). First, a court must construe the asserted claims. *See id.* Next, the trier of fact must compare the properly-construed claims to the accused infringing product. *See id.* In an infringement action brought pursuant to 35 U.S.C. § 271(e)(2)(A) – the statutory provision at issue here – the infringement inquiry is "whether, if a particular drug were put on the market, it would infringe the relevant patent." *Acorda Therapeutics Inc. v. Mylan Pharm. Inc.*, 817 F.3d 755, 760 (Fed. Cir. 2016).

B. Validity

An issued patent is presumed to be valid. *See* 35 U.S.C. § 282. To invalidate a patent, the party seeking invalidation must carry its burden of proof by "clear and convincing evidence." *See Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009). Clear and convincing evidence is evidence that "proves in the mind of the trier of fact an abiding conviction that the truth of [the] factual contentions [is] highly probable." *Intel Corp. v. U.S. Int'l Trade Comm'n*, 946 F.2d 821, 830 (Fed. Cir. 1991) (internal quotation marks omitted; first alteration in original).

III. DISCUSSION

A. Infringement

As noted previously, Lantheus concedes infringement of claims 3 and 8 of the '003 Patent if those claims are valid, but disputes infringement of claim 12 of the '276 Patent. (*Id.*; D.I. 347 at 1, 4). Curium disputes infringement of all the Asserted Claims against it. (D.I. 360).

1. "Stabilizer ... That Is Different from the First Stabilizer

ADACAP asserts that Lantheus's Product infringes claim 12 of the '276 Patent and that Curium's Product infringes claim 13 of the '276 Patent (collectively, Lantheus's Product and Curium's Product are "Defendants' Products"). The only dispute about Lantheus's infringement of claim 12 and one of several disputes about Curium's infringement of claim 13 is whether DTPA is a "stabilizer against radiolytic degradation that is different from the first stabilizer" found in claim 1, from which claims 12 and 13 depend. The Court construed "stabilizer against radiolytic degradation" to mean "an agent which protects organic molecules against radiolytic degradation" (FF ¶ 70), and the relevant parties agree that the first stabilizer in Lantheus's Product is ascorbic acid (FF ¶ 101) and in Curium's Product is sodium ascorbate (FF ¶ 137).

No documents in evidence characterize DTPA as a stabilizer in radiopharmaceuticals. The patents list a number of stabilizers but do not include DTPA as one of them. (FF ¶ 93). Instead, they describe DTPA as a "chelating agent" and a "preferred sequestering agent," defining a "sequestering agent" as "a chelating agent suitable to complex the radionuclide metal ions." (FF ¶ 106). The specification also describes using stabilizers "in a total concentration of at least 0.2 mg/mL" and up to 20 mg/mL – but it teaches using DTPA (as a chelating agent) at a fraction of that amount: "a concentration of from 0.01 to 0.10 mg/mL (preferably about 0.05 mg/mL)." (*Id.*). Similarly, Example 1 describes a ^{177}Lu-Dotatate composition containing 0.05 mg/mL of DTPA and identifies the function of DTPA as "Sequestering agent," whereas it identifies the

functions of the stabilizers gentisic acid and ascorbic acid as "RSE[s]," which stands for "Radiation Stability Enhancer[s]." (*Id.*). Both Lantheus's Product and Curium's Product use amounts of DTPA consistent with those disclosed in Example 1 (0.05 mg/mL) while using substantially more of ascorbic acid and sodium ascorbate, respectively. (FF ¶¶ 103, 138).

Additionally, when the '276 Patent specifically claims DTPA (claim 14 of the '276 Patent), it distinguished it from the claimed stabilizers. (FF ¶ 106). *See Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 130 F.4th 1372, 1379 (Fed. Cir. 2025) (explaining that, because the claim recites "four separately listed components, which include a 'VEGF antagonist' and 'a buffer[]' . . . the plain language of the claim therefore establishes a 'clear implication' that the VEGF antagonist and buffer components are distinct components of the claimed formulation"); *CAE Screenplates Inc. v. Heinrich Fiedler GmbH & Co. KG*, 224 F.3d 1308, 1317 (Fed. Cir. 2000) ("In the absence of any evidence to the contrary, we must presume that the use of these different terms in the claims connotes different meanings.").

Like the '276 patent, Defendants' respective regulatory filings (like ADACAP's) distinguish DTPA from stabilizers and describe it as a "chelating agent." (FF ¶¶ 108-109, 139-141). This evidence from the parties' FDA submissions is relevant evidence of noninfringement because "'drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA's description of the drug,' the ANDA itself dominates the analysis." *Ferring B.V. v. Watson Labs., Inc.-Florida*, 764 F.3d 1401, 1408 (Fed. Cir. 2014) (citation omitted).

In the face of this, ADACAP relies on the testimony of Drs. Price and Edwards, who agree that DTPA's molecular structure allows it to bind to free radicals, thus theoretically allowing it to

act as a stabilizer. (FF ¶¶ 111, 143).[10] Neither expert, however, did any testing of Lantheus's Product or Curium's Product to demonstrate that the DTPA in reality acts as a stabilizer in those particular formulations. (FF ¶ 144). Instead of testing, ADACAP's expert, Dr. Price, pointed to a small decline in DTPA over time in Lantheus's Product that he could not determine was statistically significant; and Dr. Price could not rule out that this decline was caused by DTPA functioning as something other than a stabilizer. (FF ¶¶ 125, 149-150). And Defendants' experts credibly explained that decrease and the bases for their opinions that other compounds perform the stabilizing work in Defendants' products. (FF ¶¶ 127-128, 150).

In view of all of the testimony and the documentary evidence, the Court cannot conclude that ADACAP has met its burden to prove that DTPA functions as a stabilizer in Defendants' Products and that either of Defendant's Products meet the "stabilizer against radiolytic degradation that is different from the first stabilizer" limitation of the claims. Therefore, the Court finds that Lantheus does not literally infringe claim 12 of the '276 Patent and that Curium does not infringe claim 13 of the '276 Patent.

2. "Stabilizers . . . in a Total Concentration

ADACAP asserts that Curium's Product infringes all Asserted Claims under the doctrine of equivalents. (D.I. 347 at 13-19). The doctrine of equivalents recognizes that the "scope of a patent is not limited to its literal terms but instead embraces all equivalents to the claims described," which includes "[u]important and insubstantial substitutes." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 731-32 (2002). The doctrine, however, is "a limited exception to the principle that claim meaning defines the scope of the exclusivity right in

[10] These experts relied on several articles, but none of those articles addresses how DTPA reacts in a pharmaceutical formulation with ascorbic acid or sodium ascorbate. (*See* FF ¶¶ 120, 147).

our patent system." *VLSI Tech. LLC v. Intel Corp.*, 87 F.4th 1332, 1341 (Fed. Cir. 2023). It "applies only in exceptional cases and is not 'simply the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims.'" *Amgen Inc. v. Sandoz, Inc.*, 923 F.3d 1023, 1029 (Fed. Cir. 2019) (quoting *London v. Carson Pirie Scott & Co.*, 946 F.2d 1534, 1538 (Fed. Cir. 1991)).

Application of the doctrine of equivalents may be limited by prosecution history estoppel. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 493 F.3d 1368, 1376 (Fed. Cir. 2007). More specifically, "[p]rosecution history estoppel applies as part of an infringement analysis to prevent a patentee from using the doctrine of equivalents to recapture subject matter surrendered from the literal scope of a claim during prosecution." *Pharma Tech. Solutions, Inc. v. LifeScan, Inc.*, 942 F.3d 1372, 1380 (Fed. Cir. 2019) (citation omitted). Prosecution history estoppel can occur in two ways: "either (1) by making a narrowing amendment to the claim ('amendment-based estoppel') or (2) by surrendering claim scope through argument to the patent examiner ('argument-based estoppel')." *Id.* (citing *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1363 (Fed. Cir. 2006)).

"With respect to amendment-based prosecution history estoppel, the Supreme Court has recognized that a 'patentee's decision to narrow his claims through amendment may be presumed to be a general disclaimer of the territory between the original claim and the amended claim.'" *Id.* (citing *Festo*, 535 U.S. at 740). "The presumption may be overcome if the patentee can show the applicability of one of several exceptions identified by the Supreme Court: (1) the equivalent was 'unforeseeable at the time of the application'; (2) 'the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question'; or (3) 'there may be some

other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question.'" *Id.* (citing *Festo*, 535 U.S. at 740-41).

Here, there is no real dispute that the amendments to the "total concentration" of stabilizers limitations in the claims of the Asserted Patents were narrowing. Prior to the amendments, all Asserted Claims recited a total stabilizer concentration of 0.2 to 20 mg/mL – a range that would have encompassed Curium's Product. (FF ¶¶ 159, 163, 189). The amendments, however, limited the "total concentration" of stabilizers to either 1.0 to 5.0 mg/mL or 0.5 mg/mL to 10.0 mg/mL, thus narrowing both the lower and upper total concentration ranges. (FF ¶ 168, 189). The amended ranges no longer literally cover Curium's Product. (*See* FF ¶ 159). ADACAP argues that these amendments do not preclude application of the doctrine of equivalents. The Court disagrees.

a. The '276 Patent

Original claim 1 of the '276 patent claimed a "total concentration" of stabilizer of "0.2 to 20 mg/mL." (FF ¶ 163). The Patent Examiner issued an Office Action rejecting claim 1 under 35 U.S.C. §103 "as being unpatentable over Chen et al. in view of Maus." (FF ¶ 164). In making that rejection, the Examiner explained that Chen discloses "[t]he gentisic acid is used in a concentration 2-20 mg/mL and ascorbic acid is used in a concentration 10 to 100 mg/mL." (FF ¶ 165). In its response to the Office Action, ADACAP narrowed the literal scope of claim 1 to recite a stabilizer concentration of "1.0 to 5.0 mg/mL." (FF ¶ 168).

In the same response, applicant argued that the amended range formed a basis to overcome the Examiner's obviousness rejection. Specifically, it argued that Chen teaches "from 8.7 to 17.8 mg/mL total concentration of stabilizers," that "[i]n comparison, the total concentration of the stabilizers recited in independent claim 1 is much lower than that of Chen (1.0 to 5.0 mg/mL total concentration of stabilizers at a volumetric radioactivity of 6.8-13.5 mCi/mL 177Lu)," and that "Chen teaches away from using such low concentration of stabilizers." (FF ¶ 169). Applicant also

argued that Maus "refers to a noticeably higher total concentration of gentisic and ascorbic acid," and "teaches away from using lower concentrations of gentisic acid and ascorbic acid." (FF ¶ 170). ADACAP further argued that "in view of the unpredictable nature of stabilizers" a person of skill in the art "would not have reasonably expected that the low total concentration of stabilizers recited in claim 1 would sufficiently stabilize the pharmaceutical aqueous solution obtained via the claimed process." (FF ¶ 171). ADACAP concluded: "Accordingly, the claimed process of making such pharmaceutical aqueous solution recited in claim 1 is nonobvious over Chen and Maus." (*Id.*). And the Patent Examiner then withdrew the obviousness rejection based on that combination of references. (FF ¶ 173).

Notwithstanding this, ADACAP argues that its amendment to the "total concentration" of stabilizer limitation simply "addressed a claim dependency rejection under Section 112." (D.I. 347 at 27). As an initial matter, even if that were true, the amendment would still have been for a substantial reason relating to patentability. *Festo*, 535 U.S. at 737 ("A patentee who narrows a claim as a condition for obtaining a patent disavows his claim to the broader subject matter, whether the amendment was made to avoid the prior art or to comply with § 112."). But ADACAP's position is not supported by applicant's contemporaneous statements during prosecution. Indeed, although applicant expressly referenced its narrowing amendment to the "total concentration" of stabilizer limitation in arguing to overcome the obviousness rejection over Chen and Maus, it did not do so in connection with the § 112 rejection. (FF ¶¶ 169-172).

ADACAP also argues that the Patent Examiner "allowed broader claims in later patents," and that this shows that the amendment narrowing the "total concentration" of stabilizer limitation during prosecution of the '276 patent was not "needed for" or "essential to patentability and cannot be the basis for estoppel." (D.I. 347 at 24). The Patent Office, however, never allowed original

claim 1 in later patents. And ADACAP does not contend that all limitations of any of the claims of the later patents literally cover Curium's product. Although the '5003 Patent claims a total concentration of stabilizer that apparently literally encompasses Curium's Product, the '5003 Patent is not asserted in this case, contains numerous other claim limitations that may distinguish it from Curium's Product, and ADACAP has not attempted to prove that Curium's Product meets the limitations of any claim in the '5003 Patent. (*See* D.I. 360 at 7-8). Without more, the Court cannot conclude that the presence of claimed stabilizer concentrations in a separate, unasserted patent with other claim limitations suggests, let alone establishes, that the narrowing amendments during prosecution of the Asserted Patents were not related to patentability.

The prosecution history thus shows that ADACAP narrowed the "total concentration" of stabilizer limitation during the prosecution of the '276 Patent to overcome the examiner's obviousness rejection over Chen and Maus – a substantial reason relating to patentability. *Festo*, 535 U.S. at 736 (explaining that "a number of statutory requirements must be satisfied before a patent can issue," including that "[t]he claimed subject matter must be useful, novel, and not obvious"). ADACAP has not rebutted the presumption that it surrendered all territory between the original and amended total concentration of stabilizer limitations – territory that covers Curium's Product. Therefore, the doctrine of equivalents is not available to ADACAP to assert infringement of the '276 Patent.

b. <u>The '003, '632 and '732 Patents</u>

In 2024, after the '276 Patent issued, ADACAP began prosecuting related applications that ultimately issued as the '003, '063, and '732 Patents. (FF ¶ 188-189). Each of those applications initially recited, in claim 1, that "stabilizer(s) against radiolytic degradation is/are present in a total concentration of 0.2 mg/mL to 20.0 mg/mL." (FF ¶ 189). Prior to any action on each of the

applications, applicant initiated an interview with the Patent Examiner, which took place on August 21, 2024. (FF ¶ 190).

The Examiner's summary of the interviews shows that during the interview, the Examiner discussed that the reasons for allowance of the previously allowed parent and/or related applications was due to the "combination of the low total concentration of stabilizers present in the pharmaceutical aqueous solution, less than 1% of EtOH in the pharmaceutical aqueous solution and/or an RCP that is maintained at greater than equal to 95% for at least 72 h when stored at 25 degrees C." (FF ¶ 191). The Examiner also stated that Maus and the de Blois reference, among others, "apply to the instant claims." (*Id.*). Thereafter, on September 10, 2024, applicant submitted amendments to each of the three applications at issue that narrowed the total stabilizer concentration range from "0.2 mg/mL to 20.0 mg/mL" to "0.5 mg/mL to 10.0 mg/mL." (FF ¶ 192).

Given the Examiner's statements, it is apparent that ADACAP amended the claims to obtain allowance over the prior art that the Examiner identified as applicable. ADACAP bears the burden of establishing that the amendments were made for some other reason. *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 33 (1997). It has not done so. "Where no explanation is established" by the patentee, as here, "the court should presume that the patent applicant had a substantial reason related to patentability for including the limiting element added by amendment." *Id.* That is true even "[w]hen the prosecution history record reveals no reason for the narrowing amendment." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1366-67 (Fed. Cir. 2003).

ADACAP argues that the amendments, at least for the '732 Patent, bore no more than a tangential relation to the equivalent in question. (D.I. 347 at 23, 27). "The tangential relation exception is 'very narrow'" and applies if the patentee can establish that "the reason for the

narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1358 (Fed. Cir. 2013) (citation omitted). Here, ADACAP narrowed the total concentration limitation to avoid the references the Examiner raised, including Maus, which ADACAP admitted disclosed "up to 15.4 mg/mL gentisic acid or 17.6 mg/mL ascorbic acid sodium salt" and therefore contained the alleged equivalent of 13-17 mg/mL of sodium ascorbate in Curium's product. (FF ¶ 170). "[A]n amendment made to avoid prior art that contains the equivalent in question is not tangential; it is central to allowance of the claim." *Festo*, 344 F.3d at 1369. Accordingly, the exception does not apply. ADACAP does not even address the amendment to the '732 patent claims, which should end the analysis.

ADACAP's reliance on "*Hakim* statements" (in which applicant told the Examiner that the invention was broader than the issued claims in the '276 Patent) is unavailing. Indeed, the case on which ADACAP relies is about claim construction, not prosecution history estoppel. *See, e.g.*, *Hakim v. Cannon Avent Group, PLC*, 479 F.3d 1313, 1318 (Fed. Cir. 2007). It would be odd indeed for this Court to find that a prosecuting party's unilateral assertion that its claim is broader than it seems allows the party to circumvent claim-narrowing amendments made during prosecution.

In any event, at best, ADACAP has shown that it may have subjectively believed the Examiner was mistaken and that the Asserted Claims would have been valid with broader claim ranges. But this subjective belief cannot shield ADACAP from the consequences of its own decisions. *See Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377-78 (Fed. Cir. 2007) ("The fact that the inventors may have thought after the fact that they could have relied on other distinctions in order to defend their claims is irrelevant and speculative; the inventors chose to distinguish over the Veber patent by narrowing the range of claimed stabilizers to exclude the

one disclosed in Veber, as well as others."); *Energy Transp. Grp. v. William Demant Holding A/S*, 697 F.3d 1342, 1360 (Fed. Cir. 2012) ("Prosecution history estoppel bars application of the doctrine of equivalents even where the applicant surrendered more claim scope than was necessary to overcome a rejection."). ADACAP chose to narrow its claims to overcome patentability rejections by the examiner. It is not permitted to artificially broaden them now.

Therefore, ADACAP's reliance on the doctrine of equivalents with respect to the "total concentration" of stabilizer limitation – which is necessary to sustain all of its infringement arguments against Curium – is barred by prosecution history estoppel as to the '003 Patent, the '632 Patent and the '732 Patent, as well as the '276 Patent.

B. Validity

1. Construction of "Pharmaceutical Aqueous Solution"

All Asserted Claims in this action either recite the term "pharmaceutical aqueous solution" or depend from claims that recite the term "pharmaceutical aqueous solution." (JTX-0001.0021; JTX-0008.0023; JTX-0007.0023; JTX-0006.0022-23). The parties dispute the term's meaning.

a. Legal Standard for Claim Construction

"[T]he ultimate question of the proper construction of the patent [is] a question of law," although subsidiary fact-finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 325 (2015). "[T]he words of a claim are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (internal citations and quotation marks omitted). Although "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding

words of the claim must also be considered. *Id.* at 1314. "[T]he 'ordinary meaning' of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321.

The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. "Even when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "'intrinsic evidence,' consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

In some cases, courts "will need to look beyond the patent's intrinsic evidence and [] consult extrinsic evidence in order to understand, for example, the background science or the

meaning of a term in the relevant art during the relevant time period." *Teva*, 574 U.S. at 331. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. Expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, although extrinsic evidence "may be useful to the court," it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

b. Claim Construction Analysis

ADACAP proposes that "pharmaceutical aqueous solution" means "a drug product suitable for commercial use and approvable by regulators." (D.I. 357 at 28). Defendants argue that the term should have its plain and ordinary meaning, i.e., a "water-based solution containing an active drug component," where the drug component "can be used as a medicine or for medicinal purposes." (D.I. 349 at 2). The Court agrees with Defendants.

Neither the intrinsic nor the extrinsic evidence supports a construction of "pharmaceutical aqueous solution" that requires a drug suitable for commercial use and approvable by regulators. The claims themselves do not reference commercial use. (FF ¶ 75). And the prosecution histories

make no reference to products ready for commercial use. (FF ¶ 79). The specification does not specially define "pharmaceutical aqueous solution." (FF ¶ 76). Instead, it defines "aqueous solution" as "a solution of one or more solute in water." (*Id.*). And it defines "pharmaceutical combination" to mean "a product that results from the mixing or combining of more than one therapeutic agent." (*Id.*).

In discussing embodiments of the "pharmaceutical aqueous solutions" of the invention, the specification describes embodiment 22b as "[t]he pharmaceutical aqueous solution according to any of the preceding embodiments, which is for commercial use." (FF ¶ 77). That embodiment, number 22b, is the first to use the words "for commercial use" in the disclosed embodiments. The addition those words in embodiment 22b, and the absence of them for other embodiments of the invention, is meaningful. It suggests that those embodiments (1 through 22a or "over 99 percent of the embodiments of the patent") do not require the disclosed pharmaceutical aqueous solution be "for commercial use." (*See* ¶ 78).

ADACAP argues that the definitions section of the specification "expressly equat[es] [a] 'pharmaceutical aqueous solution' with a 'drug product' that is 'for commercial use.'" (D.I. 357 at 28). The Court disagrees. The definition simply acknowledges that a drug product ***can*** be a pharmaceutical aqueous solution – not that ***all*** drug products are pharmaceutical aqueous solutions. And even if this Court were to accept that a pharmaceutical aqueous solution is the same thing as a drug product, it does not follow that all drug products are "for commercial use." The definition at hand contradicts this position, as it provides that only a ***subset*** of "drug products" (i.e., those in a formulation that can obtain marketing authorization) are "for commercial use."

ADACAP also argues that commercially-adjacent terms – such as "commercial drug product," "commercial scale," "manufacture[]," "shelf-life," "ready-to-use," and others – are

frequently used in the specification. (*Id.*). It is not surprising that the specification repeatedly refers to commercialization, as this is the ultimate goal of many inventions. But "it is the ***claims***, not the written description, which define the scope of the patent right." *Laitram Corp. v. NEC Corp.*, 163 F.3d 1342, 1347 (Fed. Cir. 1998) (emphasis in original). "Although the claims must be read in light of the specification, it is important that we avoid importing limitations from the specification into the claims." *Ericsson, Inc. v. D-Link Systems, Inc.*, 773 F.3d 1201, 1218 (Fed. Cir. 2014) (citation omitted); *see also Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003) ("Advantages described in the body of the specification, if not included in the claims, are not per se limitations to the claimed invention." (citation omitted)).

In light of the intrinsic evidence, the Court gives "pharmaceutical aqueous solution" its plain and ordinary meaning, i.e., a "water-based solution containing an active drug component," where the drug product is one that "can be used as a medicine or for medicinal purposes."

2. The On-Sale Bar

Under 35 U.S.C. § 102(a), a claimed invention cannot be patented if it was "on sale . . . before the effective filing date of the claimed invention." This rule, termed by courts the "on-sale bar," operates as an invalidity defense. *Sunoco Partners Mktg. & Terminals L.P. v. U.S. Venture, Inc.*, 32 F.4th 1161, 1168 (Fed. Cir. 2022). To render claims invalid under the on-sale bar, Defendants must show by clear and convincing evidence that the patented invention was both (1) "the subject of a commercial offer for sale" and (2) "ready for patenting." *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 67 (1998); *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1352 (Fed. Cir. 2002). Even "[a] single sale or offer to sell is enough to bar patentability." *Intel Corp. v. ITC*, 946 F.2d 821, 830 (Fed. Cir. 1991).

The on-sale bar does not apply if the patent owner can demonstrate that pre-critical date sales occurred "primarily for purposes of experimentation," which defeats the first prong of the test. *Allen Eng'g*, 299 F.3d at 1352-53. This experimentation exception recognizes that an inventor may delay patenting to "bring his invention to perfection, or to ascertain whether it will answer the purpose intended." *Sunoco*, 32 F.4th at 1168 (quoting *City of Elizabeth v. Am. Nicholson Pavement Co.*, 97 U.S. 126, 137 (1877)). Yet this exception is limited to sales that are primarily for experimentation – not merely sales that have some experimental value – because "[o]therwise, patent owners could acquire an undue advantage over the public by preserving their monopoly for a longer period than is allowed." *See id.* (cleaned up).

The parties here agree that the critical date here is July 25, 2017, before which any commercial, non-experimental sale of the patented invention will render the Asserted Claims invalid. (FF ⁋ 199).

a. Commercial Sale

For several years prior to the critical date, ADACAP sold thousands of doses of Lutathera to thousands of European patients. (FF ⁋⁋ 210, 220). The Lutathera subject to those sales met all of the limitations of the Asserted Claims. (FF ⁋ 202). ADACAP stipulated that the pre-critical date Lutathera met all the limitations of the Asserted Claims, except for "pharmaceutical aqueous solution" under its proposed construction of that term. (FF ⁋⁋ 200-202). The Court has now rejected ADACAP's construction, leaving the issue undisputed.

ADACAP's pre-critical date sales of Lutathera were made at prices ranging from around €4,000 to €16,000 per dose. (FF ⁋ 221). These sales are reflected in SEC filings, an internal

ADACAP spreadsheet, physician order forms, product release records, and purchase orders.[11] (FF ⁋⁋ 227-232). For example, ADACAP reported the transactions in SEC documents as "increased sales of Lutathera of €4.5 million on both named patient and compassionate use basis" in the first half of 2016 relative to the first half of 2015, explaining that "[s]ales are recognized when the following conditions are met: there is an agreement between the parties; the goods have been delivered or the services rendered; the price is fixed or can be reliably measured; and it is probable that future economic benefits from the transaction will flow to us." (FF ¶ 229). By the critical date, ADACAP had sold more than £10 million of Lutathera in the United Kingdom alone. (FF ¶ 224).

b. Experimental Use

ADACAP does not contest that there were pre-critical date sales of Lutathera or that ADACAP received compensation for those sales. Instead, it argues that the pre-critical date sales were primarily made for experimental purposes. (D.I. 357 at 17-26). Certainly, a patent owner can negate an on-sale bar by demonstrating that the sale occurred primarily for purposes of experimentation. *Sunoco*, 32 F.4th at 1168. Courts "generally look[] to objective evidence to show that a pre-critical date sale was primarily for experimentation." *Electromotive Div. of Gen. Motors Corp. v. Transportation Sys. Div. of Gen. Elec. Co.*, 417 F.3d 1203, 1212 (Fed. Cir. 2005).

ADACAP has not come forward with compelling evidence that the early Lutathera sales were for experimental purposes. Although Dr. Edwards testified that he "view[s] development as one large experiment" (FF ⁋ 239), "the question posed by the experimental use doctrine . . . is not whether the invention was under development . . . ." *Allen Eng'g*, 299 F.3d at 1354 (internal quote marks omitted). It is "whether the primary purpose of the inventor at the time of the sale, as

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[11] In many instances, ADACAP sold doses of Lutathera to distributors who then sold the doses to hospitals and patients, resulting in separate and additional sales. (FF ⁋ 222).

determined from an objective evaluation of the facts surrounding the transaction, was to conduct experimentation." *Id.*

Here, ADACAP used its expanded access programs for significant commercial benefit for many years before filing its patent application. ADACAP has not "identif[ied] any documentation of design plans or protocols for any experiments relating to manufacturing Lutathera for the expanded access programs." (FF ¶¶ 240-242). Nor did it cite "[a]ny reports of experiments completed," "[a]ny evidence that any doses were manufactured for experiments," or "any evidence that ADACAP conducted any manufacturing experiments" at all. (*Id.*). ADACAP was tracking exactly the same information after approval. (FF ¶ 242). And "[n]one of the results or learning from any of this experimentation . . . is reflected in the patents, all the data in the patents is from 2014." (FF ¶ 248).

The Federal Circuit has compiled "a list of thirteen objective factors" referred to as the *Allen Engineering* factors:

> (1) the necessity for public testing; (2) the amount of control over the experiment retained by the inventor; (3) the nature of the invention; (4) the length of the test period; (5) whether payment was made; (6) whether there was a secrecy obligation; (7) whether records of the experiment were kept; (8) who conducted the experiment; (9) the degree of commercial exploitation during testing; (10) whether the invention reasonably requires evaluation under actual conditions of use; (11) whether testing was systematically performed; (12) whether the inventor continually monitored the invention during testing; and (13) the nature of the contacts made with potential customers.

Electromotive, 417 F.3d at 1213 (citing *Allen Eng'g*, 299 F.3d at 1353). "This list is not exhaustive, and all of the experimentation factors may not apply in a particular case." *Id.* In reviewing the factors here, the Court finds that factors 1, 4, 5, 7, 9, 10, 11, and 12 are relevant but,

when viewed as a whole, do not support ADACAP's assertion that the pre-critical date sales were primarily for experimental purposes.

i. The Necessity of Public Testing (Factor 1), the Length of the Test Period (Factor 4), and Whether the Invention Reasonably Requires Evaluation under Actual Conditions of Use (Factor 10)

No public testing was necessary after September 16, 2015, the primary conclusion of ADACAP's NETTER-1 trial, because the NETTER-1 trial demonstrated the safety and efficacy of the patented form of Lutathera. (FF ¶¶ 254, 258). Although ADACAP says that it continued "experimenting" with Lutathera to "develop and validate the manufacturing process" after the conclusion of the NETTER-1 trial, the Lutathera used in the NETTER-1 trial – and in fact sold by ADACAP for years prior – met all the limitations of the Asserted Claims. (FF ¶ 200-202). It is irrelevant that ADACAP may have been refining non-patented features. *See Clock Spring, L.P. v. Wrapmaster, Inc.*, 560 F.3d 1317, 1327 (Fed. Cir. 2009) ("[T]here is no experimental use unless claimed features or overall workability are being tested for purposes of the filing of a patent application."). The NETTER-1 trial tested the claimed features of Lutathera and confirmed Lutathera's overall workability. (FF ¶¶ 200-202, 254, 258). In fact, ADACAP's own expert, Dr. Edwards, acknowledged that all the data in the Asserted Patents is from 2014. (FF ¶ 248). Therefore, by September 16, 2015, at the latest, there was no good reason for ADACAP to delay filing a patent application based on a need for further testing (let alone public testing).

Indeed, the practical reason for ADACAP's delay in filing a patent application appears to be an abrupt reversal in the company's patenting strategy. ADACAP's SEC filings from 2016 repeatedly represent that Lutathera was not, and would not, be covered by any patents. (FF ¶ 206-207). Thereafter, in 2018, Novartis acquired ADACAP (FF ¶ 208) and apparently began thinking about patent coverage changed – leading to the filing of the initial patent application more than

five years after the initial sales of the product and two years after the end of the NETTER-1 trial. (FF ¶ 209).

Looking to whether the manner of "testing" performed by ADACAP was reasonably necessary, it is noteworthy that even before the conclusion of the NETTER-1 trial, it is far from clear that charging prices for Lutathera – as ADACAP did in its expanded access programs – was ever reasonably necessary for experimentation. ADACAP seemingly could have observed the safety and efficacy of Lutathera by continuing its clinical trials. This observation is not decisive in this case, but it weighs somewhat against ADACAP.

Therefore, *Allen Engineering* factors 1, 4, and 10 do not suggest that pre-critical date sales were primarily for experimentation.

ii. Whether Payment was Made (Factor 5) and the Degree of Commercial Exploitation during Testing (Factor 9)

Prior to the critical date, ADACAP sold thousands of doses of Lutathera in Europe in expanded access programs, generating millions of British Pounds and Euros for the company. (FF ¶ 221, 225, 228). Although a high degree of commercial exploitation undermines experimentation, there does "not need to be a profit in order for there to be a sale within the meaning of section 102(b)." *In re Cygnus Telecommunications Tech., LLC, Pat. Litig.*, 536 F.3d 1343, 1355 (Fed. Cir. 2008). "Neither profit, revenue, nor even an actual sale is required for the use to be a commercial offer under section 102(b)." *Atlanta Attachment Co. v. Leggett & Platt, Inc.*, 516 F.3d 1361, 1365 (Fed. Cir. 2008). In fact, "a patent owner may have created an on-sale bar despite *losing* money on a sale." *U.S. Envtl. Prods. Inc. v. Westall,* 911 F.2d 713, 717 (Fed. Cir. 1990) (emphasis in original).

The parties dispute the degree of commercial benefit conferred by ADACAP's pre-critical date sales. Regardless of the precise amount of benefit, the pre-critical date sales of Lutathera

were "profitable" in the sense that they were a net financial positive for ADACAP. (FF ¶ 236). ADACAP received "additional financial benefits for each individual sale" of Lutathera that exceeded marginal costs. (FF ¶¶ 233-236). The sale price of Lutathera (up to €16,000) often dwarfed the marginal cost of producing a dose (around €1,440 to €2,561), leading to significant pre-critical date gross margins of roughly 70 percent. (FF ¶ 234). Although certain costs are ignored by the "marginal cost" approach, these are broadly-applicable costs, untethered to the production of individual doses of Lutathera, that would largely be incurred regardless of whether or not ADACAP made Lutathera sales through expanded access programs. (FF ¶ 235). Furthermore, ADACAP's public SEC filings touted the pre-critical date financial success of Lutathera, and ADACAP's internal presentations described pre-critical date sales of Lutathera as "profitable" and commanding a "high margin." (FF ¶¶ 227-232).

Together, this demonstrates that ADACAP intended to, and did, engage in a substantial degree of commercial exploitation and received significant commercial benefits from pre-critical date sales of Lutathera. Therefore, *Allen Engineering* factors 5 and 9 do not suggest that pre-critical date sales were primarily for experimentation.

iii. Whether Records of the Experiment were Kept (Factor 7), Whether Testing was Systematically Performed (Factor 11), and Whether the Inventor Continually Monitored the Invention during Testing (Factor 12)

As evidence that it monitored experimental use, ADACAP primarily relies on a large spreadsheet with several tabs tracking data related to the shipment and provision of expanded access doses. (FF ¶ 240-242). The spreadsheet is fairly extensive, but it does not prove as much as ADACAP suggests. It does not demonstrate records of experimentation. Indeed, it largely contains the same data that is collected for "true commercial sales." (FF ¶ 242).

ADACAP also relies "204 produced compassionate use doses" to regulatory authorities as part of obtaining regulatory approval to show records of experimentation. (FF ¶ 245). Notably, these 204 doses were all manufactured by November 16, 2015, and thus cannot show that the many sales after this date were experimental. (FF ¶ 245-246). And although the submission to regulatory authorities is a point in ADACAP's favor, it is far from enough to demonstrate that these sales were primarily experimental.

Therefore, ADACAP cannot persuasively point to evidence that testing was performed in a manner consonant with experimentation. *Allen Engineering* factors 7, 11, and 12 do not indicate that the pre-critical date sales were primarily for purposes of experimentation.

iv. Comity

ADACAP also asserts that this Court should not apply the on-sale bar here due to principles of international comity. (D.I. 357 at 31-32). Comity requires a "true conflict" between United States law and foreign law. *See Gross v. German Found. Indus. Initiative*, 456 F.3d 363, 393 (3d Cir. 2006). "Absent true conflicts, a judgment from a foreign court, or parallel proceedings in a foreign forum, rarely have United States courts abstained from deciding the merits of a case on international comity grounds." *Id.*

There is no "true conflict" here. The on-sale bar does not prohibit companies from engaging in European expanded access programs. Instead, the on-sale bar simply prevents a company from patenting an invention that it has commercially sold – at home or abroad. If companies wish to avoid the on-sale bar, they need not refrain from engaging in expanded access programs or selling their unpatented inventions abroad; they need only promptly file patent applications. *See LaBounty Mfg., Inc. v. ITC*, 958 F.2d 1066, 1071 (Fed. Cir. 1992) ("The general

purpose behind section 102(b) bars is to require inventors to assert with due diligence their right to a patent through the prompt filing of a patent application.")

c. Ready for Patenting

To prove an on-sale bar, Defendants must also show that the invention was "ready for patenting" at the time of the pre-critical date commercial sales. This showing can be made in "at least two ways: by proof of reduction to practice before the critical date; or by proof that prior to the critical date the inventor had prepared drawings or other descriptions of the invention that were sufficiently specific to enable a person skilled in the art to practice the invention." *Pfaff*, 525 U.S. at 67-68. Defendants bear the burden of demonstrating either path by clear and convincing evidence.

i. Description of the Invention

An invention is ready for patenting if there is documentation "sufficiently specific to enable a person skilled in the art to practice the invention." *Id.* Courts have found "drawings and detailed descriptions in . . . lab notebook pages" and "CAD drawings and descriptions" to be sufficient to satisfy this documentation requirement. *See Minerva Surgical, Inc. v. Hologic, Inc.*, 59 F.4th 1371, 1381 (Fed. Cir. 2023); *Hamilton Beach Brands, Inc. v. Sunbeam Prods., Inc.*, 726 F.3d 1370, 1378 (Fed. Cir. 2013). Here, we have an entire NDA filled with data and detailed descriptions of Lutathera, which was filed on March 31, 2016, more than a year before the critical date.

With one exception, there is no dispute that the NDA enables all elements of the Asserted Claims. That exception is ADACAP's argument that based solely on its construction of "pharmaceutical aqueous solution," "the claimed process is enabled only when it is able to obtain regulatory approval," which did not occur until a later date. (FF ¶¶ 200-201, 268). But this Court has rejected ADACAP's proposed claim construction and given the term its plain and ordinary

meaning. Thus, there remains no dispute that the NDA contains an enabling disclosure of the Asserted Claims.

That is hardly surprising. The NDA discloses all elements of the Asserted Claims in "copious detail," providing "a complete roadmap on how to manufacture and use Lutathera." (FF ¶¶ 265). As ADACAP's expert testified, it "definitely" contains "much more information on Lutathera and how to manufacture it than what's presented in the specification of the asserted patents," including "extensive data on actual batches of Lutathera beyond what's presented in examples 1 through 3" of the Asserted Patents. (FF ¶¶ 264 266). Indeed, the NDA discloses the composition of the drug product, the amounts of each ingredient, how to manufacture it, and stability studies, including "protocols on how to perform those stability studies, which is not provided in the patent." (FF ¶¶ 264-265).

Dr. Dick persuasively testified that the NDA as filed on March 31, 2016 was enabling under the *Wands* factors. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). "The NDA gives you the complete instructions on how to make and use Lutathera, which had already been very well developed at the time," making experimentation unnecessary; "the NDA has thousands of pages that would direct you on how to make and use Lutathera," including "multiple working examples of actual batches included in there to show you the results that you expect;" "Lutathera is a very straightforward manufacturing process" for a drug that's "[n]early identical" to the Erasmus formulation; "[p]eople had been using Lutathera for over a decade and published results on it, so there was significant prior art;" "[a] POSA would have had all of those literature publications and would have the radiochemistry skill to implement what was in the NDA;" "Lutathera was very predictable at that time through the Erasmus data, through the publications"; and "the NDA is a very predictable document because you have already developed and validated all of your

manufacturing, as well as performed at least a Phase 3 clinical trial." (FF ¶ 264). The Court agrees. The NDA was an enabling disclosure as of March 31, 2016.

ii. Reduction to Practice

"An invention is reduced to practice when the patentee has an embodiment that [i] meets every limitation and [ii] operates for its intended purpose." *Honeywell Int'l, Inc. v. Universal Avionics Sys. Corp.*, 488 F.3d 982, 997 (Fed. Cir. 2007). "[L]ater refinements do not preclude reduction to practice, [and] it is improper to conclude that an invention is not reduced to practice merely because further testing is being conducted." *Atlanta*, 516 F.3d at 1367. Here, the Lutathera provided in ADACAP's expanded access programs met every limitation of the Asserted Claims.[12] And the Lutathera sold in those programs was known to operate for its intended purpose by September 16, 2015, at the latest, when ADACAP's heralded NETTER-1 trial concluded.

"[T]he patents themselves are the most important and, indeed, most persuasive evidence of the patents' intended purpose," although it may sometimes be appropriate to consider extrinsic evidence. *Medtronic, Inc. v. Teleflex Innovations S.À.R.L.*, 68 F.4th 1298, 1304 (Fed. Cir. 2023). The inventors must be aware that the invention works for its intended purpose; thus, "[t]esting is required to demonstrate reduction to practice in some instances because without such testing there cannot be sufficient certainty that the invention will work for its intended purpose." *Z4 Techs., Inc. v. Microsoft Corp.*, 507 F.3d 1340, 1352 (Fed. Cir. 2007) (quoting *Slip Track Sys., Inc. v. Metal–Lite, Inc.*, 304 F.3d 1256, 1267 (Fed. Cir. 2002)).

ADACAP's argument on "intended purpose" here mirrors its proposed claim construction. It says that the primary purpose of Lutathera is to be "approvable by regulators." (D.I. 357 at 18).

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12 As with the enabling disclosure, ADACAP's sole argument to the contrary rests on its proposed construction of "pharmaceutical aqueous solution" – which this Court has rejected above. (D.I. 357 at 27-30).

This is unpersuasive. To begin, as explained in the context of claim construction, there is no good argument that the claims themselves require a commercial drug ready for regulatory approval. Although "the 'intended purpose' need not be stated in claim limitations that define the claim scope," the specification here cannot otherwise support ADACAP's position that the invention must be ripe for approval by regulators. *See Barry v. Medtronic, Inc.*, 914 F.3d 1310, 1325 (Fed. Cir. 2019). The primary focus of the of the specification is the radiochemical stability of the invented drug product – not regulatory approval.

It seems more sensible to embrace the intended purpose offered by Dr. Edwards, which is still generous to ADACAP. Dr. Edwards testified that "[t]he purpose of the invention was to develop an industrialized manufacturing process that would allow Lutathera to be made at a central location in high purity and high stability, and be distributed to remotely located end users." (FF ¶ 205). But as already noted, Lutathera was shown to work for this intended purpose by the end of the NETTER-1 trial. (FF ¶¶ 254, 258). Indeed, well before the end of the NETTER-1 trial, ADACAP had been manufacturing Lutathera "at commercial scale" and sending Lutathera to "remote locations." (FF ¶ 205). This already demonstrates a fair degree of confidence in the safety and efficacy of commercial-scale Lutathera.

Any remaining concerns were dispelled by the resounding success of the NETTER-1 trial. The Lutathera evaluated in the NETTER-1 trial maintained high purity and high stability. Before the end of the NETTER-1 trial, the Data Safety Monitoring Board for the trial recommended that the study be halted because it would be unethical to continue providing an inferior treatment to patients in the control group – citing to "overwhelming evidence" of the benefit of Lutathera. (FF ¶¶ 253-254). That alone showed "that clearly people believed that Lutathera worked for its intended purpose." (FF ¶ 255). To cap it off, on September 16, 2015, ADACAP announced that

the "pivotal" NETTER-1 trial had concluded and had "demonstrate[ed] a statistically significant and clinical meaningful increase in progression-free survival."[13] (FF ¶ 258).

Thus, even conservatively, the subject matter of the Asserted Claims was reduced to practice by September 16, 2015. It had already been widely manufactured, sold and administered to patients by that point. And the conclusion of the NETTER-1 trial confirmed the safety and efficacy of the drug.[14]

d. Application of the On-Sale Bar

Defendants have proven by clear and convincing evidence that the thousands of sales for millions of British Pounds and Euros over approximately five years before the critical date constitute commercial sales of Lutathera, a product that met all of the elements of the Asserted Claims. ADACAP has not shown that those sales were experimental – or anything other than the commercial "sales" they were represented to be in ADACAP's SEC statements.

Defendants have also proven by clear and convincing evidence that the subject matter of the Asserted Claims was ready for patenting well before the critical date. Indeed, the subject matter was reduced to practice by September 16, 2015 with the NETTER-1 Trial and was the subject of an enabling description of the invention in the form of the NDA by March 31, 2016.

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13 Further, even if the "intended purpose" of the invention is that it be "approvable by regulators" (this Court holds it is not), this was satisfied by ADACAP's submission of the NDA on March 31, 2016. That submission, combined with the robust data collected in the NETTER-1 trial, demonstrates that ADACAP objectively believed Lutathera could obtain regulatory approval at that point.

14 This Court recognizes that the Federal Circuit has held that "experimental use cannot occur after a reduction to practice." *In re Cygnus*, 536 F.3d at 1356 (citing *Cont'l Plastic Containers v. Owens Brockway Plastic Prods., Inc.*, 141 F.3d 1073, 1079 (Fed.Cir.1998)). This is a separate ground that independently justifies application of the on-sale bar rule here. For completeness, however, this Court has conducted a more fulsome on-sale bar analysis.

Each of the many sales between these dates and the critical date triggered the on-sale bar. Thus, all the Asserted Claims are invalid.

IV. CONCLUSION

After considering the entire record and applicable law, the Court concludes that (1) Lantheus's Product infringes claims 3 and 8 of the '003 Patent but does not infringe claim 12 of the '276 Patent; (2) Curium's Product does not infringe any of the Asserted Claims; and (3) all Asserted Claims are invalid under 35 U.S.C. § 102(a) for being on sale more than a year before the effective filing date of the claimed inventions.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ADVANCED ACCELERATOR APPLICATIONS, USA, INC., and ADVANCED ACCELERATOR APPLICATIONS, SA, Plaintiffs, v. LANTHEUS MEDICAL IMAGING, INC., LANTHEUS HOLDINGS, INC, Defendants.	)	C.A. No. 24-95 (MN)
ADVANCED ACCELERATOR APPLICATIONS, USA, INC., and ADVANCED ACCELERATOR APPLICATIONS, SA, Plaintiffs, v. CURIUM US LLC, CURIUM US HOLDINGS LLC, CURIUM NETHERLANDS BV, and CURIUM INTERNATIONAL TRADING BV, Defendants.	)	C.A. No. 24-1161 (MN) CONSOLIDATED

ORDER

At Wilmington, this 17th day of June 2026, IT IS HEREBY ORDERED that the Court will hold a teleconference with Plaintiffs and the Lantheus Defendants at 9:30 a.m. on June 18, 2026 to discuss Plaintiffs' Motion for Injunctive Relief Against Lantheus (D.I. 379). Defendants shall circulate call in information.

The Honorable Maryellen Noreika
United States District Judge