IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT MASSACHUSETTS

RADIUS HEALTH INC. and IPSEN PHARMA S.A.S., Plaintiffs, v. ORBICULAR PHARMACEUTICAL TECHNOLOGIES PRIVATE LIMITED, Defendant.	Civil Action No. 1:22-CV-11546-RGS

ORBICULAR PHARMACEUTICAL TECHNOLOGIES PRIVATE LIMITED'S ANSWER TO SECOND AMENDED COMPLAINT

Orbicular Pharmaceutical Technologies Private Limited ("Orbicular" or "Defendant") answers and responds to the Second Amended Complaint of Plaintiffs Radius Health, Inc. ("Radius") and Ipsen Pharma S.A.S. ("Ipsen") (collectively "Radius or "Plaintiffs") as follows:

NATURE OF THE ACTION

1. This is a civil action for patent infringement arising under the patent laws of the United States, Title 35 of the United States Code, including 35 U.S.C. § 271(e)(2)(A). This action relates to Abbreviated New Drug Application ("ANDA") No. 217245, filed by and for the benefit of Defendant with the United States Food and Drug Administration ("FDA") ("ANDA No. 217245"). Through ANDA No. 217245, Defendant seeks to market generic versions of Tymlos® (abaloparatide) (the "ANDA Product"), prior to the expiration of U.S. Patent Nos. RE49,444 (the "'444 patent"), 8,148,333 (the "'333 patent"), 8,748,382 (the "'382 patent") 10,996,208 (the "'208 patent"), and 11,782,041 (the "'041 patent") (collectively, the "Patents-in-Suit").

ANSWER:

Orbicular admits the Second Amended Complaint alleges this is a civil action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, including 35 U.S.C. § 271(e)(2)(A). Orbicular admits this action relates to Abbreviated New Drug Application ("ANDA") No. 217245, filed by Defendant with the United States Food and Drug Administration ("FDA") ("ANDA No. 217245" or "Orbicular's ANDA"). Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval, for the matters described therein, prior to the expiration of U.S. Patent Nos. RE49,444 ("the '444 patent"), 8,148,333 ("the '333 patent"), 8,748,382 ("the '382 patent"), 10,996,208 ("the '208 patent") and 11,782,041 ("the '041 patent") (collectively, the "Patents-in-Suit"). Orbicular denies the remaining allegations in Paragraph 1 of the Second Amended Complaint.

THE PARTIES

2. Plaintiff Radius is a Massachusetts-based corporation, having its principal place of business at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210. Radius is organized and existing under the laws of the State of Delaware. Radius is a science-driven fully integrated biopharmaceutical company that is committed to developing and commercializing innovative endocrine and other therapeutics.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 2 of the Second Amended Complaint and, on that basis, denies them.

3. Radius is the holder of New Drug Application ("NDA") No. 208743, which was approved by the FDA for the manufacture and sale of Tymlos® (abaloparatide) on April 28, 2017.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 3 of the Second Amended Complaint and, on that basis, denies them.

4. Tymlos® (abaloparatide) is approved for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Tymlos® (abaloparatide) reduces the risk of vertebral and nonvertebral fractures.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 4 of the Second Amended Complaint and, on that basis, denies them.

5. The FDA granted approval based on positive results from two landmark clinical trials in osteoporosis patients that were sponsored by Radius. Specifically, results reported at 18 months from the human clinical trial known as the ACTIVE Trial and from the first six months of the ACTIVExtend Trial demonstrated consistent significant and rapid reductions in the risk of vertebral and nonvertebral fractures in participating osteoporosis patients regardless of age, years since menopause, presence or absence of prior fracture (vertebral or nonvertebral) and bone mineral density (BMD) at baseline. At approval, Tymlos® (abaloparatide) was the first new anabolic (bone building) agent for postmenopausal women with osteoporosis in the United States in nearly fifteen years.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 5 of the Second Amended Complaint and, on that basis, denies them.

6. Radius is an owner and assignee of each of the Patents-in-Suit, which are listed in the FDA's publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book") as covering the Tymlos® (abaloparatide) product. Radius possesses the right to sue for and obtain equitable relief and damages for infringement of the Patents-in-Suit.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to whether Radius is an owner and assignee of each of the Patents-in-Suit and denies this allegation on this basis. Orbicular admits the FDA's publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book") speaks for itself. Orbicular denies infringement of the Patents-in-Suit and denies Radius is entitled to obtain any relief or alleged damages for alleged infringement of the Patents-in-Suit. Orbicular denies the remaining allegations in Paragraph 6 of the Second Amended Complaint.

7. Plaintiff Ipsen is a limited company incorporated under French law, having its principal place of business at 65 Quai George Gorse, 92100 Boulogne-Billancourt, France. Ipsen is a specialty-driven biopharmaceutical company that develops and markets new medicines, including biological drugs, for the treatment of debilitating diseases in various therapeutic areas.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 7 of the Second Amended Complaint and, on that basis, denies them.

8. Ipsen is a co-owner of the '444 patent '333 patent, and '382 patent. Beginning in 2005, Radius and Ipsen collaborated on the development of the abaloparatide formulations and methods

of treatment that are the subject of the '444 patent, '333 patent, and '382 patent. Radius retained the rights to develop, manufacture, and distribute the abaloparatide formulations.

ANSWER:

Orbicular admits the '444 patent, '333 patent, and '382 patent are documents that speak for themselves. Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the remaining allegations contained in Paragraph 8 of the Second Amended Complaint and, on that basis, denies them.

9. Upon information and belief, Defendant Orbicular is incorporated in India with its principal place of business at P. No. 53, ALEAP Industrial Estate, Behind Pragati Nagar Kukatpally, Hyderabad, 500 090 Telangana, India. On information and belief, Orbicular has no place of business in the United States.

ANSWER:

Orbicular admits it is an India business entity with a place of business at P. No. 53, ALEAP Industrial Estate, Behind Pragati Nagar Kukatpally, Hyderabad, 500 090 Telangana, India. Whether Orbicular does or does not have a place of business in the United States is a conclusion of law to which no response is required. To the extent a further response is required Orbicular denies the remaining allegations contained in Paragraph 9 of the Second Amended Complaint.

10. Orbicular has designated the following agent in the United States as authorized to accept service of process: Andrew J. Miller, Esq., Windels Marx Lane & Mittendorf, LLP, 1 Giralda Farms, Suite 100, Madison, New Jersey, 07940.

ANSWER:

Orbicular admits that, with respect to Orbicular's ANDA, pursuant to 21 C.F.R. § 314.95(c)(9) Orbicular designated Andrew J. Miller, Esq., Windels Marx Lane & Mittendorf, LLP, 1 Giralda Farms, Suite 100, Madison, New Jersey, 07940 (e-mail: amiller@windelsmarx.com) as an agent in the United States, authorized to accept service of process. Orbicular denies the remaining allegations in Paragraph 10 of the Second Amended Complaint.

11. Upon information and belief, Orbicular is in the business of, among other things, the development and manufacture of generic and specialty pharmaceutical products for sale throughout the United States, including in Massachusetts.

ANSWER:

Orbicular admits it manufactures and/or markets pharmaceutical products. Orbicular denies the remaining allegations in Paragraph 11 of the Second Amended Complaint.

12. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the Federal Food, Drug, and Cosmetic Act ("FD&C Act") (codified at 21 U.S.C. § 355(j)). ANDA No. 217245 included a paragraph IV certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") to, *inter alia*, U.S. Patent No. 7,803,770 (the "'770 patent"), which reissued as the '444 patent on March 7, 2023, the '333 patent, '382 patent, and '208 patent. Upon information and belief, Defendant will amend ANDA No. 217245 to contain a Paragraph IV Certification that includes the '041 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular admits Orbicular's ANDA No. 217245 included a paragraph IV certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") to each of U.S. Patent 7,803,770 ("the '770 patent"), and the '333, '382 and '208 patents. Orbicular's ANDA will address the '041 patent as needed. Orbicular denies the remaining allegations in Paragraph 12 of the Second Amended Complaint.

13. Defendant mailed a Notice of Paragraph IV Certification Re: Orbicular Pharmaceutical Technologies Private Limited's Abaloparatide Injection, 3120 MCG / 1.56 ML (2000 MCG/ML); U.S. Patent Nos. 7,803,770; 8,148,333; 8,748,382; 10,996,208; and 11,255,842 ("Notice Letter") to Radius and Ipsen. The Notice Letter is dated August 8, 2022 and was mailed to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210, among others. Radius and Ipsen received the Notice Letter on August 9, 2022 and commenced this action within 45 days of receiving the Notice Letter. Upon information and belief, Defendant will send another Notice of Paragraph IV Certification notifying Radius and Ipsen that it amended ANDA No. 217245 to contain a Paragraph IV Certification that includes the '041 patent.

ANSWER:

Orbicular admits its Notice Letter dated August 8, 2022 is a document that speaks for itself, that its Notice Letter was sent to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 and to Ipsen, among others, and that its Notice Letter was received by Radius and Ipsen on August 9, 2022 and that the Complaint in this action was filed within 45 days of August 9, 2022. Orbicular's ANDA will address the '041 patent as needed Orbicular denies the remaining allegations in Paragraph 13 of the Second Amended Complaint.

14. Upon information and belief, Defendant developed the ANDA Product that is the subject of ANDA No. 217245. Defendant submitted ANDA No. 217245 to the FDA, seeking approval to market and sell the ANDA Product throughout the United States, including in Massachusetts.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 14 of the Second Amended Complaint.

15. ANDA No. 217245 seeks approval to commercially manufacture, use, offer for sale, sell, and/or import a generic version of Radius's Tymlos® (abaloparatide) prior to the expiration of the Patents-in-Suit.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein, prior to the expiration of the '770, '333, '382 and '208 patents. Orbicular denies the remaining allegations in Paragraph 15 of the Second Amended Complaint.

ALLEGATIONS OF JURISDICTION AND VENUE

16. This is a complaint for patent infringement under the patent laws of the United States, Title 35 U.S.C. § 100 *et seq.*, including 35 U.S.C. § 271(e)(2)(A), arising out of the submission of ANDA No. 217245 to the FDA.

ANSWER:

Orbicular admits the Second Amended Complaint alleges this is a civil action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, including 35 U.S.C. § 271(e)(2)(A), allegedly arising out of the submission of Orbicular's ANDA to the FDA. To the extent a further response is required Orbicular denies the remaining allegations in Paragraph 16 of the Second Amended Complaint.

17. This Court has subject matter jurisdiction of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

ANSWER:

Paragraph 17 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required, for purposes of this action only, Orbicular does not contest subject matter jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 17 of the Second Amended Complaint.

18. This Court has personal jurisdiction over Defendant at least because, upon information and belief: (i) Defendant, directly or through its affiliates, develops, manufactures, imports, markets, offers to sell, sells, and/or distributes generic pharmaceutical products throughout the United States, including in Massachusetts, and therefore does business in Massachusetts, derives revenue from conducting business in Massachusetts, and maintains continuous and systematic contacts with Massachusetts; and (ii) Defendant has committed, induced, or contributed to acts of patent infringement in Massachusetts by submitting ANDA No. 217245 that includes a Paragraph IV Certification (a technical act of infringement under 35 U.S.C. § 271(e)(2)(A)) that Defendant seeks to import, offer for sale, and sell its ANDA Product throughout the United States, including in this judicial district, before the expiration of the Patents-in-Suit.

ANSWER:

Paragraph 18 of the Second Amended Complaint contains legal conclusions to which no response is required. Orbicular denies it has committed, induced, or contributed to acts of patent infringement with respect to the Patents-in-Suit. Orbicular admits it filed Orbicular's ANDA, a document that speaks for itself, with the FDA seeking approval, for the matters described therein,

prior to the expiration of the '770, '333, '382 and '208. To the extent any further response is required, for purposes of this action only, Orbicular does not contest personal jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 18 of the Second Amended Complaint.

19. This Court has personal jurisdiction over Defendant at least because, upon information and belief, if ANDA No. 217245 is approved, the ANDA Product will be manufactured, marketed, sold, distributed, imported, and/or used by Defendant throughout the United States, including in Massachusetts; prescribed by physicians practicing in Massachusetts; and/or administered to patients in Massachusetts, all of which would have a substantial effect on Massachusetts. For example, upon information and belief, Defendant knows that Tymlos® (abaloparatide) has been and will be distributed and used in Massachusetts. Upon information and belief, and because of, among other things, the Commonwealth's generic substitution laws, upon approval of its ANDA, Defendant intends to replace Tymlos® (abaloparatide) sales with its generic drug as set forth in its ANDA.

ANSWER:

Paragraph 19 of the Second Amended Complaint contains legal conclusions to which no response is required. Orbicular admits it filed Orbicular's ANDA, a document that speaks for itself. To the extent any further response is required, for purposes of this action only, Orbicular does not contest personal jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 19 of the Second Amended Complaint.

20. This Court has personal jurisdiction over Defendant at least because Defendant has used the statutory process for challenging infringement and/or validity of the '770 patent/'444 patent, '333 patent, '382 patent, and '208 patent by filing a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) and sending notice of such certification to the NDA holder, which triggers patent litigation. With knowledge of this statutory process, Defendant sent the Notice Letter to Radius at its principal place of business in Massachusetts, knowing that such certification could trigger a patent infringement suit to protect Radius's patent rights in this judicial district. Upon information and belief, Defendant will use the same statutory process for challenging infringement and/or validity of the '041 patent by filing another certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) and sending notice of such certification to the NDA holder. Upon information and belief, with knowledge of this statutory process, Defendant will send another Notice Letter to Radius at its principal place of business in Massachusetts, knowing that such certification could trigger a patent infringement suit to protect Radius's patent rights in this judicial district.

ANSWER:

Paragraph 20 of the Second Amended Complaint contains legal conclusions to which no response is required. Orbicular admits it filed Orbicular's ANDA, a document that speaks for itself. Orbicular's ANDA will address the '041 patent as needed. To the extent any further response is required, for purposes of this action only, Orbicular does not contest personal jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 20 of the Second Amended Complaint.

21. In the alternative, Defendant is subject to jurisdiction throughout the United States, and specifically in the Commonwealth of Massachusetts pursuant to Fed. R. Civ. P. 4(k)(2) because (a) these claims arise under federal law; (b) Defendant would be a foreign defendant not subject to personal jurisdiction in the courts of any state; and (c) Defendant has sufficient contacts with the United States as a whole, including, but not limited to, filing ANDAs with the FDA and, upon information and belief, manufacturing and selling generic pharmaceutical products that are distributed throughout the United States, such that this Court's exercise of jurisdiction over Defendant satisfies due process and is otherwise consistent with the United States Constitution and laws.

ANSWER:

Paragraph 21 of the Second Amended Complaint contains legal conclusions to which no response is required. Orbicular admits it filed Orbicular's ANDA, a document that speaks for itself. To the extent any further response is required, for purposes of this action only, Orbicular does not contest personal jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 21 of the Second Amended Complaint.

22. For the reasons set forth above, and for additional reasons which will be supplied if Defendant challenges personal jurisdiction in this action, Defendant is subject to personal jurisdiction in this District.

ANSWER:

Paragraph 22 of the Second Amended Complaint contains legal conclusions to which no response is required. Orbicular admits it filed Orbicular's ANDA, a document that speaks for

itself. To the extent any further response is required, for purposes of this action only, Orbicular does not contest personal jurisdiction in this Court. Orbicular denies the remaining allegations of Paragraph 22 of the Second Amended Complaint.

23. Venue is proper in this Court under 28 U.S.C. §§ 1391 and/or 1400(b) because Defendant is a foreign corporation that does not have a state of residence in the United States.

ANSWER:

Paragraph 23 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent any further response is required, for purposes of this action only, Orbicular does not contest venue in this Court. Orbicular denies the remaining allegations of Paragraph 23 of the Second Amended Complaint.

ALLEGED FACTS AS TO ALL COUNTS

The Patents-in-Suit

24. The '444 patent, the '333 patent, and the '382 patent are assigned to Radius and Ipsen. The '208 patent and '041 patent are assigned to Radius. As of the date of this Second Amended Complaint, Radius holds the rights to enforce the Patents-in-Suit against potential infringers in the United States and to seek damages.

ANSWER:

Orbicular denies Radius or Ipsen is entitled to obtain any relief or alleged damages for alleged infringement of the Patents-in-Suit and denies Orbicular is a potential infringer of the Patents-in-Suit. Orbicular lacks knowledge or information sufficient to form a belief as to the remaining allegations in Paragraph 24 of the Second Amended Complaint and denies on this basis.

25. The Patents-in-Suit are valid, enforceable, and have not expired.

ANSWER:

Orbicular denies the Patents-in-Suit are valid or enforceable. Orbicular lacks knowledge or information sufficient to form a belief as to whether the Patent-in-Suit have expired and denies

on this basis. Orbicular denies the remaining allegations in Paragraph 25 of the Second Amended Complaint.

26. The '444 patent, entitled "Method of Treating Osteoporosis Comprising Administration of PTHRP Analog," is a reissue of the '770 patent, which was duly and legally issued on September 28, 2010. The '444 patent was duly and legally issued on March 7, 2023. Upon issuance of the '444 patent, Plaintiffs surrendered the '770 patent under 35 U.S.C. § 252. The '444 patent claims, *inter alia*, methods of treating osteoporosis comprising daily subcutaneous administration of compositions comprising 80 μg of abaloparatide to a human in need thereof. The '444 patent contains all of the claims that previously issued as the '770 patent plus certain additional claims. A copy of the '444 patent is attached as Exhibit A.

ANSWER:

Orbicular admits the '444 patent is a document that speaks for itself and that the Second Amended Complaint purports to attach a copy of the '444 patent as Exhibit A. Orbicular denies the '444 patent was duly and legally issued. To the extent a further response is required, Orbicular denies the remaining allegations in Paragraph 26 of the Second Amended Complaint.

27. The '333 patent, entitled "Stable Composition Comprising a PTHRP Analogue," was duly and legally issued on April 3, 2012. The '333 patent claims, *inter alia*, storage-stable compositions suitable for administration to a subject comprising abaloparatide and an effective amount of a pH buffer to maintain the pH in a range of about 4.5 to about 5.6, or wherein said pH is about 5.1. A copy of the '333 patent is attached as Exhibit B.

ANSWER:

Orbicular admits the '333 patent is a document that speaks for itself and that the Second Amended Complaint purports to attach a copy of the '333 patent as Exhibit B. Orbicular denies the '333 patent was duly and legally issued. To the extent a further response is required, Orbicular denies the remaining allegations in Paragraph 27 of the Second Amended Complaint.

28. The '382 patent, entitled "Method of Drug Delivery for Bone Anabolic Protein," was duly and legally issued on June 10, 2014. The '382 patent claims, *inter alia*, methods of stimulating bone growth in a subject in need thereof comprising administering to said subject storage-stable compositions comprising abaloparatide and an effective amount of buffer to maintain the pH in a range of about 4.5 to about 5.6. A copy of the '382 patent is attached as Exhibit C.

ANSWER:

Orbicular admits the '382 patent is a document that speaks for itself and that the Second Amended Complaint purports to attach a copy of the '382 patent as Exhibit C. Orbicular denies the '382 patent was duly and legally issued. To the extent a further response is required, Orbicular denies the remaining allegations in Paragraph 28 of the Second Amended Complaint.

29. The '208 patent, entitled "Abaloparatide Formulations and Methods of Testing, Storing, Modifying, and Using Same," was duly and legally issued on May 4, 2021. The '208 patent claims, *inter alia*, formulated abaloparatide drug products comprising ≤5% or ≤1.0% w/w beta-Asp10 of the total peptide content, methods of analyzing abaloparatide comprising detecting and quantifying the presence of ≤5% or ≤1.0% w/w beta-Asp10 of the total peptide content, and methods of establishing the suitability of a formulated abaloparatide drug product for administration to a subject comprising detecting and quantifying the presence of ≤5% w/w beta-Asp10 of the total peptide content. A copy of the '208 patent is attached as Exhibit D.

ANSWER:

Orbicular admits the '208 patent is a document that speaks for itself and that the Second Amended Complaint purports to attach a copy of the '208 patent as Exhibit D. Orbicular denies the '208 patent was duly and legally issued. To the extent a further response is required, Orbicular denies the remaining allegations in Paragraph 29 of the Second Amended Complaint.

30. The '041 patent, entitled "Abaloparatide Formulations and Methods of Testing, Storing, Modifying, and Using Same," was duly and legally issued on October 10, 2023. The '041 patent claims, *inter alia*, novel formulated abaloparatide drug products having low levels (e.g., ≤ 3%) of beta-Asp10, and methods of treating a subject in need thereof by administering said drug products having said low levels of beta-Asp10 at a daily dose of about 80 µg of abaloparatide. A copy of the '041 patent is attached as Exhibit E.

ANSWER:

Orbicular admits the '041 patent is a document that speaks for itself and that the Second Amended Complaint purports to attach a copy of the '041 patent as Exhibit E. Orbicular denies the '041 patent was duly and legally issued. To the extent a further response is required, Orbicular denies the remaining allegations in Paragraph 30 of the Second Amended Complaint.

Allegations Regards Tymlos® (abaloparatide)

31. Tymlos® (abaloparatide) is a human parathyroid hormone related peptide [PTHrP (1-34)] analog indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture. The recommended dose of Tymlos® (abaloparatide) is 80 mcg subcutaneously once daily.

ANSWER:

Orbicular admits the FDA-approved Label for Tymlos® is a document that speaks for itself. To the extent a further response is required Orbicular denies the remaining allegations in Paragraph 31 of the Second Amended Complaint.

32. According to the Tymlos® (abaloparatide) label, "Dosage Forms and Strengths," 3120 mcg/1.56 mL (2000 mcg/mL) is provided in a single-patient-use prefilled pen. The prefilled pen delivers 30 daily doses of 80 mcg abaloparatide in 40 mcL of sterile, clear, colorless solution.

ANSWER:

Orbicular admits the FDA-approved Label for Tymlos® is a document that speaks for itself. To the extent a further response is required Orbicular denies the remaining allegations in Paragraph 32 of the SecondAmended Complaint.

33. Tymlos® (abaloparatide) is sold and marketed in the United States under NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 33 of the Second Amended Complaint and, on that basis, denies them.

34. Radius is the holder of NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 34 of the Second Amended Complaint and, on that basis, denies them.

35. Tymlos® (abaloparatide), its method of manufacture, and its FDA-approved use are each covered by at least one claim of the Patents-in-Suit.

ANSWER:

Orbicular admits the Patents-in-Suit are documents that speak for themselves. To the extent a further response is required Orbicular denies the remaining allegations in Paragraph 35 of the Second Amended Complaint.

36. The Patents-in-Suit are listed in the FDA's Orange Book in conjunction with NDA No. 208743.

ANSWER:

Admitted on information and belief as of the date the Second Amended Complaint was filed the Patents-in-Suit were listed in the FDA's Orange Book in conjunction with NDA No. 208743. Orbicular denies the remaining allegations in Paragraph 36 of the Second Amended Complaint.

Allegations Regarding ANDA No. 217245

37. Defendant sent the Notice Letter to Radius and Ipsen, dated August 8, 2022 and received by Radius and Ipsen on August 9, 2022, purportedly pursuant to § 505(j)(2)(B)(ii) and § 505(j)(2)(B)(iv) of the FD&C Act and 21 C.F.R. § 314.95, regarding ANDA No. 217245. The Notice Letter was signed by Louis H. Weinstein of the law firm Windels Marx Lane & Mittendorf, LLP on behalf of Defendant.

ANSWER:

Orbicular admits its Notice Letter regarding Orbicular's ANDA, dated August 8, 2022 and signed by Louis H. Weinstein of the law firm Windels Marx Lane & Mittendorf, LLP as outside counsel for Defendant, is a document that speaks for itself, that it was sent pursuant to at least § 505(j)(2)(B)(ii) and § 505(j)(2)(B)(iv) of the FD&C Act and 21 C.F.R. § 314.95, that its Notice Letter was sent to Defendant and that its Notice Letter was received by Defendant on August 9,

2022. Orbicular denies the remaining allegations in Paragraph 37 of the Second Amended Complaint.

38. Defendant's Notice Letter states that ANDA No. 217245 has been submitted with a Paragraph IV Certification to obtain approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the '770 patent, '333 patent, '382 patent, and '208 patent.

ANSWER:

Orbicular admits that Orbicular's Notice Letter is a document that speaks for itself, and that among other statements it states: "Orbicular seeks to obtain approval to engage in the commercial manufacture, use or sale of Orbicular's proposed product before the expiration of U.S. Patent Nos.: 7,803,770; 8,148,333; 8,748,382; 10,996,208; and 11,255,842." Orbicular denies the remaining allegations in Paragraph 38 of the Second Amended Complaint.

39. The Notice Letter states that ANDA No. 217245 was submitted with a Paragraph IV Certification pursuant to § 505(j)(2)(A)(vii)(IV) of the FD&C Act and 21 C.F.R. § 314.94(a)(12)(i)(A)(4) alleging that the '770 patent, '333 patent, '382 patent, and '208 patent are invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the ANDA Product.

ANSWER:

Orbicular admits that Orbicular's Notice Letter is a document that speaks for itself, and that among other statements it states: "Pursuant to § 505(j)(2)(B)(ii) and § 505(j)(2)(B)(iv) of the Federal Food, Drug and Cosmetic Act ("the Act") and § 314.95 of Title 21 of the Code of Federal Regulations ("C.F.R."), please be advised that Orbicular Pharmaceutical Technologies Private Limited ("Orbicular") has filed patent certifications pursuant to § 505(j)(2)(A)(vii)(IV) of the Act and § 314.94(a)(12)(i)(A)(4) of Title 21 of the C.F.R. in support of Orbicular's Abbreviated New Drug Application ("ANDA") No. 217245 with respect to Orbicular's proposed Abaloparatide Injection, 3120 mcg / 1.56 mL (2000 mcg/mL) ("Orbicular's proposed product")." Orbicular denies the remaining allegations in Paragraph 39 of the Second Amended Complaint.

40. In view of Defendant's Notice Letter and Paragraph IV Certification regarding the '770 patent, '333 patent, '382 patent, and '208 patent contained in ANDA No. 217245, Defendant had knowledge of the '770 patent, '333 patent, '382 patent, and '208 patent at least since the date on which Defendant filed ANDA No. 217245 with the FDA.

ANSWER:

Orbicular admits it had knowledge of the '770 patent, '333 patent, '382 patent, and '208 patent at least since the date on which Orbicular filed ANDA No. 217245 with the FDA. Orbicular denies the remaining allegations in Paragraph 40 of the Second Amended Complaint.

41. ANDA No. 217245 refers to and relies upon the NDA for Tymlos® (abaloparatide), NDA No. 208743, and contains data that, according to Defendant, demonstrate the bioequivalence of the ANDA Product and Tymlos® (abaloparatide). *See* 21 U.S.C. § 355(j)(2); 21 C.F.R. § 314.94(a)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. To the extent the allegations of Paragraph 41 of the Second Amended Complaint are consistent with Orbicular's ANDA Orbicular admits those allegations. Orbicular denies the remaining allegations in Paragraph 41 of the Second Amended Complaint.

42. The Notice Letter states that the active ingredient in the ANDA Product is abaloparatide.

ANSWER:

Orbicular admits that Orbicular's Notice Letter is a document that speaks for itself, and that among other statements it states: "The active ingredient present in Orbicular's proposed product is a synthetic 34 amino acid peptide with the amino acid sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-Arg-Glu-Leu-Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2, commonly known as abaloparatide and the dosage form is an

injection solution for subcutaneous use." Orbicular denies the remaining allegations in Paragraph 42 of the Second Amended Complaint.

43. Upon information and belief, the label for the ANDA Product will recommend the same Indication and Usage as Tymlos® (abaloparatide).

ANSWER:

Orbicular admits that the proposed Label in Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 43 of the Second Amended Complaint.

44. Upon information and belief, the label for the ANDA Product will reference the same Clinical Studies as Tymlos® (abaloparatide).

ANSWER:

Orbicular admits that the proposed Label in Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 44 of the Second Amended Complaint.

45. Upon information and belief, the label for the ANDA Product will recommend the same Dosage and Administration as Tymlos® (abaloparatide).

ANSWER:

Orbicular admits that the proposed Label in Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 45 of the Second Amended Complaint.

46. Upon information and belief, administration of the ANDA Product, like Tymlos® (abaloparatide), will be used for the treatment of postmenopausal women with osteoporosis at high risk for fracture.

ANSWER:

Orbicular admits that the proposed Label in Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 46 of the Second Amended Complaint.

47. Pursuant to 21 U.S.C. § 355(b)(1), the '382 patent and '333 patent were submitted to the FDA with NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 47 of the Second Amended Complaint and, on that basis, denies them.

48. Pursuant to 21 C.F.R. § 314.53(c)(2), Form FDA 3542 for the '208 patent was submitted to the FDA in connection with NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 48 of the Second Amended Complaint and, on that basis, denies them.

49. Pursuant to 21 C.F.R. § 314.53(c)(2), Form FDA 3542 for the '444 patent was submitted to the FDA in connection with NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 49 of the Second Amended Complaint and, on that basis, denies them.

50. Pursuant to 21 C.F.R. § 314.53(c)(2), Form FDA 3542 for the '041 patent was submitted to the FDA in connection with NDA No. 208743.

ANSWER:

Orbicular lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in Paragraph 50 of the Second Amended Complaint and, on that basis, denies them.

51. This action is being commenced within 45 days from the date Radius and Ipsen received Defendant's Notice Letter, which was August 9, 2022.

ANSWER:

Orbicular admits that the Complaint in this action was filed within 45 days from the date Radius and Ipsen received Orbicular's Notice Letter, which was August 9, 2022. Orbicular denies the remaining allegations in Paragraph 51 of the Second Amended Complaint.

52. Initiating this action within 45 days of receipt of the Notice Letter triggers a 30-month stay of regulatory approval of Defendant's ANDA. *See* 21 U.S.C. § 355 (j)(5)(B)(iii).

ANSWER:

Paragraph 52 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required, Orbicular denies the allegations of Paragraph 52 of the Second Amended Complaint.

53. Plaintiffs are entitled to full relief from Defendant's acts of infringement, including entry of judgment that any final approval of ANDA No. 217245 shall be effective no earlier than the expiration date of the last to expire of the Patents-in-Suit, or any later expiration of exclusivity for the Patents-in-Suit to which Plaintiffs are or may become entitled. *See* 35 U.S.C. § 271(e)(4).

ANSWER:

Denied.

COUNT I: ALLEGED INFRINGEMENT OF U.S. PATENT NO. RE49,444

54. Plaintiffs repeat and re-allege each of the foregoing paragraphs as if fully set forth herein.

ANSWER:

Orbicular repeats and re-alleges its Answers to each of the foregoing Paragraphs as if fully set forth herein.

55. Upon information and belief, Defendant prepared ANDA No. 217245.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 55 of the Second Amended Complaint.

56. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the FD&C Act (codified at 21 U.S.C. § 355(j)) for the purpose of seeking FDA approval to market the ANDA Product prior to the expiration of the '770 patent, which has since reissued as the '444 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that the '770 patent, the '444 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 56 of the Second Amended Complaint.

57. ANDA No. 217245 is based upon Tymlos® (abaloparatide), as its reference-listed drug.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 57 of the Second Amended Complaint.

58. The ANDA Product is an abaloparatide product.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 58 of the Second Amended Complaint.

59. Defendant submitted ANDA No. 217245 with a Paragraph IV Certification to the '770 patent for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, sale, offering for sale, and/or importation of the ANDA Product throughout the United States before the expiration of the '770 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein before the expiration of the '770 patent and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 59 of the Second Amended Complaint.

60. The '770 patent reissued as the '444 patent on March 7, 2023. Under 35 U.S.C. § 252, Plaintiffs surrendered the '770 patent upon issuance of the '444 patent. The '444 patent includes all of the original claims of the '770 patent and sixty-five additional claims.

ANSWER:

Orbicular admits that the '770 patent and the '444 patent are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 60 of the Second Amended Complaint.

61. Under 21 U.S.C. § 355(j)(2)(B), the filer of an ANDA containing a paragraph IV certification must provide notice of the filing to each patent owner and each NDA holder. Under 21 U.S.C. § 355(j)(2)(B)(iv)(II), such notice must "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." Likewise, 21 C.F.R. § 314.95(c)(7) requires that such notice include a "detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement must include: "For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed" and "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation." 21 C.F.R. § 314.95(c)(7)(i)–(ii).

ANSWER:

Paragraph 61 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required Orbicular denies the remaining allegations of Paragraph 61 of the Second Amended Complaint.

62. As of the date of the Notice Letter, Defendant was aware of the statutory provisions and regulations set out in 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R. § 314.95(c)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 62 of the Second Amended Complaint.

63. Purportedly in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95, Defendant sent a copy of the Notice Letter to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210, which was received on August 9, 2022. Defendant also sent a copy to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, which was received on August 9, 2022.

ANSWER:

Orbicular admits its Notice Letter dated August 8, 2022 is a document that speaks for itself, that its Notice Letter was sent in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 and to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, among others, and that its Notice Letter was received by Radius and Ipsen on August 9, 2022. Orbicular denies the remaining allegations in Paragraph 63 of the Second Amended Complaint.

64. Under 35 U.S.C. § 271(e)(2)(A), Defendant's submission of ANDA No. 217245 with a Paragraph IV Certification to the '770 patent, which since reissued as the '444 patent, for the purpose of obtaining approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the patent constitutes infringement of one or more claims of the '770 patent, including at least claim 1. Because the '444 patent includes all of the original claims in the '770 patent, and supersedes the '770 patent, Defendant's submission of ANDA No. 217245 with a Paragraph IV Certification to the '770 patent also constitutes infringement of the '444 patent.

ANSWER:

Orbicular denies it has infringed any valid claim of the '770 patent or the '444 patent. Orbicular denies the remaining allegations in Paragraph 64 of the Second Amended Complaint.

65. For example, claim 1 of the '444 patent (which is identical to claim 1 of the original '770 patent) claims "[a] method of treating osteoporosis comprising daily subcutaneous administration of a composition comprising 80 µg of [$Glu^{22,25}$, $Leu^{23,28,31}$, Aib^{29}, $Lys^{26,30}$]hPTHrP(l-34)NH_2 to a human in need thereof." As set forth in Defendant's Notice Letter, the active ingredient in the ANDA Product is abaloparatide, i.e., "a synthetic 34 amino acid peptide with the amino acid sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-Arg-Glu-Leu-Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2[.]" The Notice Letter also provides that the ANDA Product is "an injection solution for subcutaneous use." The Notice Letter further provides that "the indicated dosage of Orbicular's proposed product [the ANDA Product] will be 80 µg per day and Orbicular's proposed product will deliver 80 µg." The Notice Letter does not assert that use of the ANDA Product does not infringe any of the claims of the '770 patent, and therefore likewise cannot be construed to assert that the use of the ANDA Product does not infringe any of the identical claims of the '444 patent, including, for example, claim 1.

ANSWER:

Orbicular admits that the '770 patent, the '444 patent and Orbicular's Notice Letter are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 65 of the Second Amended Complaint.

66. Treatment with Tymlos® (abaloparatide) results in practicing at least the method of claim 1 of the '444 patent. By its ANDA submission, Defendant has necessarily represented to the FDA that the ANDA Product will be the same as Tymlos® (abaloparatide). Accordingly, on information and belief, the ANDA Product label will instruct, e.g., patients, prescribers, and physicians to follow the claimed "method of treating osteoporosis comprising daily subcutaneous administration of a composition comprising 80 µg of [$Glu^{22,25}$, $Leu^{23,28,31}$, Aib^{29}, $Lys^{26,30}$]hPTHrP(l-34)NH_2 to a human in need thereof." On information and belief, patients, prescribers, and physicians will follow instructions in the ANDA Product label and will infringe at least claim 1 of the '444 patent. By submitting an ANDA with a label that, on information and belief, is the same as the Tymlos® (abaloparatide) label, Defendant is knowingly inducing third parties to infringe at least claim 1 of the '444 patent. Therefore, on information and belief, Defendant knowingly infringes, induces others to infringe, and/or contributes to third-party infringement of at least claim 1 of the '444 patent.

ANSWER:

Orbicular admits that the '770 patent, the '444 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies it infringed any valid claim of the '770 patent or the '444 patent. Orbicular denies it infringes, induces others to infringe, and/or contributes to third-party infringement of any claim of the '770 patent or the '444 patent. Orbicular denies the remaining allegations in Paragraph 66 of the Second Amended Complaint.

67. Upon information and belief, Defendant will commercially manufacture, use, offer to sell, and/or sell within the United States, and/or import into the United States the ANDA Product if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 67 of the Second Amended Complaint.

68. Upon information and belief, Defendant will instruct, e.g., patients, prescribers, and healthcare providers to use the ANDA Product in accordance with the proposed product labeling if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 68 of the Second Amended Complaint.

69. Upon information and belief, Defendant's commercial manufacture, use, offering to sell and/or sale within the United States, and/or importation into the United States of the ANDA Product would infringe, directly and/or indirectly, one or more of the '444 patent claims under 35 U.S.C. § 271.

ANSWER:

Denied.

70. Upon information and belief, by commercially offering for sale and/or selling the ANDA Product in accordance with its label, Defendant would knowingly induce and/or contribute to third-party infringement of one or more claims of the '444 patent under 35 U.S.C. § 271.

ANSWER:

Denied.

71. Defendant had knowledge of the original claims of the '444 patent since at least the time it filed ANDA No. 217245 with a Paragraph IV Certification and is knowingly infringing the claims in the '444 patent.

ANSWER:

Orbicular admits it had knowledge of the '770 patent since at least the time it filed Orbicular's ANDA. Orbicular denies it is infringing the '444 patent. Orbicular denies the remaining allegations in Paragraph 71 of the Second Amended Complaint.

72. Defendant's statements of the factual and legal bases for its opinion regarding the non-infringement of the '770 patent, and thus the '444 patent, are devoid of any objective good-faith basis in either the facts or the law.

ANSWER:

Denied.

73. Defendant acted without a reasonable basis for believing that it would not be liable for infringing, actively inducing infringement of, and/or contributing to infringement by others of the '770 patent and therefore the '444 patent.

ANSWER:

Denied.

74. This case therefore is "exceptional," and Plaintiffs are entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

ANSWER:

Denied.

75. The acts of infringement of the '444 patent set forth above will cause Plaintiffs to suffer irreparable harm for which there is no adequate remedy at law, unless Defendant is preliminarily and permanently enjoined by this Court.

ANSWER:

Denied.

76. Plaintiffs are entitled to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an Order of this Court that the effective date of the FDA's final approval of ANDA No. 217245 be a date that is not earlier than the expiration date of the '444 patent, or any later expiration of exclusivity for the '444 patent to which Plaintiffs are or may become entitled.

ANSWER:

Denied.

COUNT II: ALLEGED INFRINGEMENT OF U.S. PATENT NO. 8,148,333

77. Plaintiffs repeat and re-allege each of the foregoing Paragraphs as if fully set forth herein.

ANSWER:

Orbicular repeats and re-alleges its Answers to each of the foregoing Paragraphs as if fully set forth herein.

78. Upon information and belief, Defendant prepared ANDA No. 217245.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 78 of the Second Amended Complaint.

79. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the FD&C Act (codified at 21 U.S.C. § 355(j)) for the purpose of seeking FDA approval to market the ANDA Product prior to the expiration of the '333 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 79 of the Second Amended Complaint.

80. ANDA No. 217245 is based upon Tymlos® (abaloparatide), as its reference listed drug.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 80 of the Second Amended Complaint.

81. The ANDA Product is an abaloparatide product.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 81 of the Second Amended Complaint.

82. Defendant submitted ANDA No. 217245 with a Paragraph IV Certification to the '333 patent for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, sale, offering for sale, and/or importation of the ANDA Product throughout the United States before the expiration of the '333 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein before the expiration of the '333 patent and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 82 of the Second Amended Complaint.

83. Under 21 U.S.C. § 355(j)(2)(B), the filer of an ANDA containing a paragraph IV certification must provide notice of the filing to each patent owner and each NDA holder. Under 21 U.S.C. § 355(j)(2)(B)(iv)(II), such notice must "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." Likewise, 21 C.F.R. § 314.95(c)(7) requires that such notice include a "detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement must include: "For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed" and "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation." 21 C.F.R. § 314.95(c)(7)(i)–(ii).

ANSWER:

Paragraph 83 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required Orbicular denies the remaining allegations of Paragraph 83 of the Second Amended Complaint.

84. As of the date of the Notice Letter, Defendant was aware of the statutory provisions and regulations set out in 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R. § 314.95(c)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 84 of the Second Amended Complaint.

85. Purportedly in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95, Defendant sent a copy of the Notice Letter to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 which was received on August 9, 2022. Defendant also sent a copy to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, which was received on August 9, 2022.

ANSWER:

Orbicular admits its Notice Letter dated August 8, 2022 is a document that speaks for itself, that its Notice Letter was sent in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 and to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, among others, and that its Notice Letter was received by Radius and Ipsen on August 9, 2022. Orbicular denies the remaining allegations in Paragraph 85 of the Second Amended Complaint.

86. Under 35 U.S.C. § 271(e)(2)(A), Defendant's submission of ANDA No. 217245 with a Paragraph IV Certification to the '333 patent for the purpose of obtaining approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the '333 patent constitutes infringement of one or more claims of the '333 patent, including at least claim 1.

ANSWER:

Orbicular denies it has infringed any valid claim of the '333 patent. Orbicular denies the remaining allegations in Paragraph 86 of the Second Amended Complaint.

87. For example, claim 1 of the '333 patent claims "[a] storage-stable composition suitable for administration to a subject comprising: a) a PTHrP analogue having the sequence [$Glu^{22,25}$, $Leu2^{3,28,31}$, Aib^{29}, $Lys^{26,30}$] hPTHrP(l-34)NH_2 (SEQ ID NO.2); and b) an effective amount of a pH buffer to maintain the pH in a range of about 4.5 to about 5.6." As set forth in Defendant's Notice Letter, the active ingredient in the ANDA Product is abaloparatide, i.e., "a synthetic 34 amino acid peptide with the amino acid sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-Arg-Glu-Leu-Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2[.]" The Notice Letter does not assert that the ANDA Product does not infringe any of the claims of the '333 patent, including, for example, claim 1.

ANSWER:

Orbicular admits that the '333 patent and Orbicular's Notice Letter are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 87 of the Second Amended Complaint.

88. Tymlos® (abaloparatide) embodies the storage-stable composition claimed in at least claim 1 of the '333 patent. By its ANDA submission, Defendant has necessarily represented to the FDA that the ANDA Product will be the same as Tymlos® (abaloparatide), including, on information and belief, that the ANDA Product is "[a] storage-stable composition suitable for administration to a subject comprising: a) a PTHrP analogue having the sequence [$Glu^{22,25}$, $Leu^{23,28,31}$, Aib^{29}, $Lys^{26,30}$] hPTHrP(l-34)NH_2 (SEQ ID NO.2); and b) an effective amount of a pH buffer to maintain the pH in a range of about 4.5 to about 5.6." By filing an ANDA with a Paragraph IV Certification with respect to the '333 patent, Defendant has committed an act of infringement pursuant to 35 U.S.C. § 271(e)(2)(A). Therefore, on information and belief, Defendant infringes at least claim 1 of the '333 patent.

ANSWER:

Orbicular admits that the '333 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies it infringed any valid claim of the '333 patent or that it infringes any claim of the '333 patent. Orbicular denies the remaining allegations in Paragraph 88 of the Second Amended Complaint.

89. Upon information and belief, Defendant will commercially manufacture, use, offer to sell, and/or sell within the United States, and/or import into the United States the ANDA Product if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 89 of the Second Amended Complaint.

90. Upon information and belief, Defendant will instruct, e.g., patients, prescribers, and healthcare providers to use the ANDA Product in accordance with the proposed product labeling if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 90 of the Second Amended Complaint.

91. Upon information and belief, Defendant's commercial manufacture, use, offering to sell and/or sale within the United States, and/or importation into the United States of the ANDA Product would infringe, directly and/or indirectly, one or more of the '333 patent claims under 35 U.S.C. § 271.

ANSWER:

Denied.

92. Defendant had knowledge of the '333 patent since at least the time it filed ANDA No. 217245 with a Paragraph IV Certificate and is knowingly infringing the '333 patent.

ANSWER:

Orbicular admits it had knowledge of the '333 patent since at least the time it filed Orbicular's ANDA. Orbicular denies it is infringing the '333 patent. Orbicular denies the remaining allegations in Paragraph 92 of the Second Amended Complaint.

93. Defendant's statements of the factual and legal bases for its opinion regarding the non-infringement of the '333 patent contained in Defendant's Notice Letter are devoid of any objective good-faith basis in either the facts or the law.

ANSWER:

Denied.

94. Defendant acted without a reasonable basis for believing that it would not be liable for infringing the '333 patent, actively inducing infringement of the '333 patent, and/or contributing to infringement by others of the '333 patent.

ANSWER:

Denied.

95. This case therefore is "exceptional," and Plaintiffs are entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

ANSWER:

Denied.

96. The acts of infringement of the '333 patent set forth above will cause Plaintiffs to suffer irreparable harm for which there is no adequate remedy at law, unless Defendant is preliminarily and permanently enjoined by this Court.

ANSWER:

Denied.

97. Plaintiffs are entitled to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an Order of this Court that the effective date of the FDA's final approval of ANDA No. 217245 be a date that is not earlier than the expiration date of the '333 patent, or any later expiration of exclusivity for the '333 patent to which Plaintiffs are or may become entitled.

ANSWER:

Denied.

COUNT III: ALLEGED INFRINGEMENT OF U.S. PATENT NO. 8,748,382

98. Plaintiffs repeat and re-allege each of the foregoing paragraphs as if fully set forth herein.

ANSWER:

Orbicular repeats and re-alleges its Answers to each of the foregoing Paragraphs as if fully set forth herein.

99. Upon information and belief, Defendant prepared ANDA No. 217245.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 99 of the Second Amended Complaint.

100. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the FD&C Act (codified at 21 U.S.C. § 355(j)) for the purpose of seeking FDA approval to market the ANDA Product prior to the expiration of the '382 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 100 of the Second Amended Complaint.

101. ANDA No. 217245 is based upon Tymlos® (abaloparatide), as its reference listed drug.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 101 of the Second Amended Complaint.

102. The ANDA Product is an abaloparatide product.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 102 of the Second Amended Complaint.

103. Defendant submitted ANDA No. 217245 with a Paragraph IV Certification to the '382 patent for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, sale, offering for sale, and/or importation of the ANDA Product throughout the United States before the expiration of the '382 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein before the expiration of the '382 patent and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 103 of the Second Amended Complaint.

104. Under 21 U.S.C. § 355(j)(2)(B), the filer of an ANDA containing a paragraph IV certification must provide notice of the filing to each patent owner and each NDA holder. Under 21 U.S.C. § 355(j)(2)(B)(iv)(II), such notice must "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." Likewise, 21 C.F.R. § 314.95(c)(7) requires that such notice include a "detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement must include: "For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed" and "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation." 21 C.F.R. § 314.95(c)(7)(i)–(ii).

ANSWER:

Paragraph 104 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required Orbicular denies the remaining allegations of Paragraph 104 of the Second Amended Complaint.

105. As of the date of the Notice Letter, Defendant was aware of the statutory provisions and regulations set out in 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R. § 314.95(c)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 105 of the Second Amended Complaint.

106. Purportedly in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95, Defendant sent a copy of the Notice Letter to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210, which was received on August 9, 2022. Defendant also sent a copy to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, which was received on August 9, 2022.

ANSWER:

Orbicular admits its Notice Letter dated August 8, 2022 is a document that speaks for itself, that its Notice Letter was sent in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 and to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, among others, and that its Notice Letter was received by Radius and Ipsen on August 9, 2022. Orbicular denies the remaining allegations in Paragraph 106 of the Second Amended Complaint.

107. Under 35 U.S.C. § 271(e)(2)(A), Defendant's submission of ANDA No. 217245 with a Paragraph IV Certification to the '382 patent for the purpose of obtaining approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the '382 patent constitutes infringement of one or more claims of the '382 patent, including at least claim 1.

ANSWER:

Orbicular denies it has infringed any valid claim of the '382 patent. Orbicular denies the remaining allegations in Paragraph 107 of the Second Amended Complaint.

108. For example, claim 1 of the '382 patent claims "[a] method of stimulating bone growth in a subject in need thereof comprising administering to said subject a storage stable composition comprising: a) a PTHrP having the sequence [$Glu^{22,25}$, $Leu^{23,28,31}$, Aib^{29}, $Lys^{26,30}$]hPTHrP(l-34)NH_2 (SEQ ID NO.: 2); and b) an effective amount of buffer to maintain the pH in a range of about 4.5 to about 5.6." As set forth in Defendant's Notice Letter, the active ingredient in the ANDA Product is abaloparatide, i.e., "a synthetic 34 amino acid peptide with the amino acid

sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-Arg-Glu-Leu-Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2[.]" The Notice Letter does not assert that use of the ANDA Product does not infringe many claims in the '382 patent, including, for example, claim 1.

ANSWER:

Orbicular admits that the '382 patent and Orbicular's Notice Letter are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 108 of the Second Amended Complaint.

109. Treatment with Tymlos® (abaloparatide) results in practicing at least the method of claim 1 of the '382 patent. By its ANDA submission, Defendant has necessarily represented to the FDA that the ANDA Product will be the same as Tymlos® (abaloparatide). Accordingly, on information and belief, the ANDA Product label will instruct, e.g., patients, prescribers, and physicians to follow the claimed "method of stimulating bone growth in a subject in need thereof comprising administering to said subject a storage stable composition comprising: a) a PTHrP having the sequence [$Glu^{22,25}$, $Leu^{23,28,31}$, Aib^{29}, $Lys^{26,30}$]hPTHrP(l-34)NH_2 (SEQ ID NO.: 2); and b) an effective amount of buffer to maintain the pH in a range of about 4.5 to about 5.6." On information and belief, patients, prescribers, and physicians will follow instructions in the ANDA Product label and will infringe at least claim 1 of the '382 patent. By submitting an ANDA with a label that, on information and belief, is the same as the Tymlos® (abaloparatide) label, Defendant is knowingly inducing third parties to infringe at least claim 1 of the '382 patent. By filing an ANDA with a Paragraph IV Certification with respect to the '382 patent, Defendant has also committed an act of infringement pursuant to 35 U.S.C. § 271(e)(2)(A). Therefore, on information and belief, Defendant knowingly infringes, induces others to infringe, and/or contributes to third-party infringement of at least claim 1 of the '382 patent.

ANSWER:

Orbicular admits that the '382 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies it infringed any valid claim of the '382 patent. Orbicular denies it infringes, induces others to infringe, and/or contributes to third-party infringement of any claim of the '382 patent. Orbicular denies the remaining allegations in Paragraph 109 of the Second Amended Complaint.

110. Upon information and belief, Defendant will commercially manufacture, use, offer to sell, and/or sell within the United States, and/or import into the United States the ANDA Product if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 110 of the Second Amended Complaint.

111. Upon information and belief, Defendant will instruct, e.g., patients, prescribers, and healthcare providers to use the ANDA Product in accordance with the proposed product labeling if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 111 of the Second Amended Complaint.

112. Upon information and belief, Defendant's commercial manufacture, use, offering to sell and/or sale within the United States, and/or importation into the United States of the ANDA Product would infringe, directly and/or indirectly, one or more of the '382 patent claims under 35 U.S.C. § 271.

ANSWER:

Denied.

113. Upon information and belief, by commercially offering for sale and/or selling the ANDA Product in accordance with its label, Defendant would knowingly induce and/or contribute to third-party infringement of one or more claims of the '382 patent under 35 U.S.C. § 271.

ANSWER:

Denied.

114. Defendant had knowledge of the '382 patent since at least the time it filed ANDA No. 217245 with a Paragraph IV Certification and is knowingly infringing the '382 patent.

ANSWER:

Orbicular admits it had knowledge of the '382 patent since at least the time it filed Orbicular's ANDA. Orbicular denies it is infringing the '382 patent. Orbicular denies the remaining allegations in Paragraph 114 of the Second Amended Complaint.

115. Defendant's statements of the factual and legal bases for its opinion regarding the non-infringement of the '382 patent contained in Defendant's Notice Letter are devoid of any objective good-faith basis in either the facts or the law.

ANSWER:

Denied.

116 Defendant acted without a reasonable basis for believing that it would not be liable for infringing the '382 patent, actively inducing infringement of the '382 patent, and/or contributing to infringement by others of the '382 patent.

ANSWER:

Denied.

117 This case therefore is "exceptional," and Plaintiffs are entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

ANSWER:

Denied.

118. The acts of infringement of the '382 patent set forth above will cause Plaintiffs to suffer irreparable harm for which there is no adequate remedy at law, unless Defendant is preliminarily and permanently enjoined by this Court.

ANSWER:

Denied.

119. Plaintiffs are entitled to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an Order of this Court that the effective date of the FDA's final approval of ANDA No. 217245 be a date that is not earlier than the expiration date of the '382 patent, or any later expiration of exclusivity for the '382 patent to which Plaintiffs are or may become entitled.

ANSWER:

Denied.

COUNT IV: ALLEGED INFRINGEMENT OF U.S. PATENT NO. 10,996,208

120. Plaintiff Radius repeats and re-alleges each of the foregoing paragraphs as if fully set forth herein.

ANSWER:

Orbicular repeats and re-alleges its Answers to each of the foregoing Paragraphs as if fully set forth herein.

121. Upon information and belief, Defendant prepared ANDA No. 217245.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 121 of the Second Amended Complaint.

122. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the FD&C Act (codified at 21 U.S.C. § 355(j)) for the purpose of seeking FDA approval to market the ANDA Product prior to the expiration of the '208 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 122 of the Second Amended Complaint.

123. ANDA No. 217245 is based upon Tymlos® (abaloparatide), as its reference listed drug.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 123 of the Second Amended Complaint.

124. The ANDA Product is an abaloparatide product.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 124 of the Second Amended Complaint.

125. Defendant submitted ANDA No. 217245 with a Paragraph IV Certification to the '208 patent for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, sale, offering for sale, and/or importation of the ANDA Product throughout the United States before the expiration of the '208 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein before the expiration of the '208 patent and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 125 of the Second Amended Complaint.

126. Under 21 U.S.C. § 355(j)(2)(B), the filer of an ANDA containing a paragraph IV certification must provide notice of the filing to each patent owner and each NDA holder. Under 21 U.S.C. § 355(j)(2)(B)(iv)(II), such notice must "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." Likewise, 21 C.F.R. § 314.95(c)(7) requires that such notice include a "detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement must include: "For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed" and "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation." 21 C.F.R. § 314.95(c)(7)(i)–(ii).

ANSWER:

Paragraph 126 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required Orbicular denies the remaining allegations of Paragraph 126 of the Second Amended Complaint.

127. As of the date of the Notice Letter, Defendant was aware of the statutory provisions and regulations set out in 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R. § 314.95(c)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 127 of the Second Amended Complaint.

128. Purportedly in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95, Defendant sent a copy of the Notice Letter to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210, which was received on August 9, 2022. Defendant also sent a copy to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, which was received on August 9, 2022.

ANSWER:

Orbicular admits its Notice Letter dated August 8, 2022 is a document that speaks for itself, that its Notice Letter was sent in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 to Radius at 22 Boston Wharf Road, 7th Floor, Boston, Massachusetts 02210 and to Ipsen at 65 Quai Georges Corse, Boulogne-Billancourt 92100, France, among others, and that its Notice Letter was received by Radius and Ipsen on August 9, 2022. Orbicular denies the remaining allegations in Paragraph 128 of the Second Amended Complaint.

129. Under 35 U.S.C. § 271(e)(2)(A), Defendant's submission of ANDA No. 217245 with a Paragraph IV Certification to the '208 patent for the purpose of obtaining approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the '208 patent constitutes infringement of one or more claims of the '208 patent, including at least claim 14.

ANSWER:

Orbicular denies it has infringed any valid claim of the '208 patent. Orbicular denies the remaining allegations in Paragraph 129 of the Second Amended Complaint.

130. For example, claim 14 of the '208 patent claims "[a] formulated abaloparatide drug product comprising ≤5% w/w beta-Asp10 of the total peptide content, and an aqueous buffer having a pH from 4.5-5.5, wherein said formulated abaloparatide drug product has an abaloparatide concentration of between 1.8 mg/mL and 2.2 mg/mL, wherein the suitability of the formulated abaloparatide drug product for administration to a subject has been established by a method comprising: detecting and quantifying the presence of ≤5% w/w beta-Asp10 of the total peptide content in the formulated abaloparatide drug product." As set forth in Defendant's Notice Letter, the active ingredient in the ANDA Product is abaloparatide, i.e., "a synthetic 34 amino acid peptide with the amino acid sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-Arg-Glu-Leu-Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2[.]" The Notice Letter does not assert that the ANDA Product does not infringe multiple claims of the '208 patent, including, for example, claim 14.

ANSWER:

Orbicular admits that the '208 patent and Orbicular's Notice Letter are documents that speak for themselves. Orbicular denies the remaining allegations in Paragraph 130 of the Second Amended Complaint.

131. Tymlos® (abaloparatide) embodies the formulated abaloparatide drug product claimed in at least claim 14 of the '208 patent. By its ANDA submission, Defendant has necessarily represented to the FDA that the ANDA Product will be the same as Tymlos® (abaloparatide), including, on information and belief, that the ANDA Product is "[a] formulated abaloparatide drug product comprising ≤5% w/w beta-Asp10 of the total peptide content, and an aqueous buffer having a pH from 4.5-5.5, wherein said formulated abaloparatide drug product has an abaloparatide concentration of between 1.8 mg/mL and 2.2 mg/mL, wherein the suitability of the formulated abaloparatide drug product for administration to a subject has been established by a method comprising: detecting and quantifying the presence of ≤5% w/w beta-Asp10 of the total peptide content in the formulated abaloparatide drug product." By filing an ANDA with a Paragraph IV Certification with respect to the '208 patent, Defendant has committed an act of infringement pursuant to 35 U.S.C. § 271(e)(2)(A). Therefore, on information and belief, Defendant knowingly infringes at least claim 14 of the '208 patent.

ANSWER:

Orbicular admits that the '208 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies it infringed any valid claim of the '208 patent. Orbicular denies it

infringes any claim of the ‘208 patent. Orbicular denies the remaining allegations in Paragraph 131 of the Second Amended Complaint.

132. Upon information and belief, Defendant will commercially manufacture, use, offer to sell, and/or sell within the United States, and/or import into the United States the ANDA Product if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular’s ANDA with the FDA seeking approval for the matters described therein and that Orbicular’s ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 132 of the Second Amended Complaint.

133. Upon information and belief, Defendant will instruct, e.g., patients, prescribers, and healthcare providers to use the ANDA Product in accordance with the proposed product labeling if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular’s ANDA with the FDA seeking approval for the matters described therein and that Orbicular’s ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 133 of the Second Amended Complaint.

134. Upon information and belief, Defendant’s commercial manufacture, use, offering to sell and/or sale within the United States, and/or importation into the United States of the ANDA Product would infringe, directly and/or indirectly, one or more of the '208 patent claims under 35 U.S.C. § 271.

ANSWER:

Denied.

135. Upon information and belief, by commercially offering for sale and/or selling the ANDA Product in accordance with its label, Defendant would knowingly induce and/or contribute to third-party infringement of one or more claims of the '208 patent under 35 U.S.C. § 271.

ANSWER:

Denied.

136. Defendant had knowledge of the '208 patent since at least the time it filed ANDA No. 217245 with a Paragraph IV Certification and is knowingly infringing the '208 patent.

ANSWER:

Orbicular admits it had knowledge of the '208 patent since at least the time it filed Orbicular's ANDA. Orbicular denies it is infringing the '208 patent, knowingly or otherwise. Orbicular denies the remaining allegations in Paragraph 136 of the Second Amended Complaint.

137. Defendant's statements of the factual and legal bases for its opinion regarding the non-infringement of the '208 patent contained in Defendant's Notice Letter are devoid of any objective good-faith basis in either the facts or the law.

ANSWER:

Denied.

138. Defendant acted without a reasonable basis for believing that it would not be liable for infringing the '208 patent, actively inducing infringement of the '208 patent, and/or contributing to infringement by others of the '208 patent.

ANSWER:

Denied.

139. This case therefore is "exceptional," and Radius is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

ANSWER:

Denied.

140. The acts of infringement of the '208 patent set forth above will cause Radius to suffer irreparable harm for which there is no adequate remedy at law, unless Defendant is preliminarily and permanently enjoined by this Court.

ANSWER:

Denied.

141 Radius is entitled to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an Order of this Court that the effective date of the FDA's final approval of ANDA No. 217245 be a date that is not earlier than the expiration date of the '208 patent, or any later expiration of exclusivity for the '208 patent to which Radius is or may become entitled.

ANSWER:

Denied.

COUNT V: ALLEGED INFRINGEMENT OF U.S. PATENT NO. 11,782,041

142. Plaintiff Radius repeats and re-alleges each of the foregoing paragraphs as if fully set forth herein.

ANSWER:

Orbicular repeats and re-alleges its Answers to each of the foregoing Paragraphs as if fully set forth herein.

143. Upon information and belief, Defendant prepared ANDA No. 217245.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 143 of the Second Amended Complaint.

144. Defendant submitted ANDA No. 217245 to the FDA pursuant to § 505(j) of the FD&C Act (codified at 21 U.S.C. § 355(j)) for the purpose of seeking FDA approval to market the ANDA Product prior to the expiration of the '041 patent.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 144 of the Second Amended Complaint.

145. ANDA No. 217245 is based upon Tymlos® (abaloparatide), as its reference listed drug.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 145 of the Second Amended Complaint.

146. The ANDA Product is an abaloparatide product.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 146 of the Second Amended Complaint.

147. Upon information and belief, Defendant will amend ANDA No. 217245 to contain a Paragraph IV Certification that includes the '041 patent for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, sale, offering for sale, and/or importation of the ANDA Product throughout the United States before the expiration of the '041 patent.

ANSWER:

Orbicular's ANDA will address the '041 patent as needed. Orbicular denies the remaining allegations in Paragraph 147 of the Second Amended Complaint.

148. Under 21 U.S.C. § 355(j)(2)(B), the filer of an ANDA containing a paragraph IV certification must provide notice of the filing to each patent owner and each NDA holder. Under 21 U.S.C. § 355(j)(2)(B)(iv)(II), such notice must "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." Likewise, 21 C.F.R. § 314.95(c)(7) requires that such notice include a "detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement must include: "For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed" and "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation." 21 C.F.R. § 314.95(c)(7)(i)–(ii).

ANSWER:

Paragraph 148 of the Second Amended Complaint contains legal conclusions to which no response is required. To the extent an answer is required Orbicular denies the remaining allegations of Paragraph 148 of the Second Amended Complaint.

149. As of the date of the Notice Letter, Defendant was aware of the statutory provisions and regulations set out in 21 U.S.C. § 355(j)(2)(B)(iv)(II) and 21 C.F.R. § 314.95(c)(7).

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 149 of the Second Amended Complaint.

150. Upon information and belief, in accordance with 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95, Defendant will send another Notice of Paragraph IV Certification notifying Radius and Ipsen that it amended ANDA No. 217245 to contain a Paragraph IV Certification that includes the '041 patent.

ANSWER:

Orbicular's ANDA will address the '041 patent as needed. Orbicular denies the remaining allegations in Paragraph 150 of the Second Amended Complaint.

151. Under 35 U.S.C. § 271(e)(2)(A), Defendant's submission of ANDA No. 217245 for the purpose of obtaining approval to engage in the commercial manufacture, use, or sale of the ANDA Product before the expiration of the '041 patent constitutes infringement of one or more claims of the '041 patent, including at least claim 4.

ANSWER:

Orbicular denies it has infringed any valid claim of the '041 patent. Orbicular denies the remaining allegations in Paragraph 151 of the Second Amended Complaint.

152. For example, claim 4 of the '041 patent claims "[a] method of treating a subject in need thereof, the method comprising administering to the subject in need thereof the formulated abaloparatide drug product according to any one of claims 1 to 3, at a daily dosage of about 80 µg of abaloparatide." Claim 1 of the '041 patent, from which claim 4 depends, claims "[a] formulated abaloparatide drug product comprising an aqueous buffer, wherein said formulated abaloparatide

drug product has an abaloparatide concentration of between 1.8 mg/mL and 2.2 mg/mL, wherein said formulated abaloparatide drug product has a pH from 4.5-5.5, and wherein said formulated abaloparatide drug product comprises ≤3% w/w of beta-Asp10, based on a total peptide content of the formulated abaloparatide drug product."

ANSWER:

Orbicular admits that the '041 patent is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 152 of the Second Amended Complaint.

153. As set forth in Defendant's Notice Letter, the active ingredient in the ANDA Product is abaloparatide, i.e., "a synthetic 34 amino acid peptide with the amino acid sequence: Ala-Val-Ser-Glu-His-Gln-Leu-Leu-His-Asp-Lys-Gly-Lys-Ser-Ile-Gln-Asp-Leu-Arg-Arg-ArgGlu-Leu Leu-Glu-Lys-Leu-Leu-Aib-Lys-Leu-His-Thr-Ala-NH_2[.]" Upon information and belief, the supplemental Notice Letter will not assert that the ANDA Product does not infringe multiple claims of the '041 patent, including, for example, claim 4.

ANSWER:

Orbicular admits that Orbicular's Notice Letter is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 153 of the Second Amended Complaint.

154. Treatment with Tymlos® (abaloparatide) results in practicing at least the method of claim 4 of the '041 patent. By its ANDA submission, Defendant has necessarily represented to the FDA that the ANDA Product will be the same as Tymlos® (abaloparatide), including, on information and belief, that the ANDA Product is "[a] formulated abaloparatide drug product comprising an aqueous buffer, wherein said formulated abaloparatide drug product has an abaloparatide concentration of between 1.8 mg/mL and 2.2 mg/mL, wherein said formulated abaloparatide drug product has a pH from 4.5-5.5, and wherein said formulated abaloparatide drug product comprises ≤3% w/w of beta-Asp10, based on a total peptide content of the formulated abaloparatide drug product." Accordingly, on information and belief, the ANDA Product label will instruct, e.g., patients, prescribers, and physicians to follow the claimed "method of treating a subject in need thereof, the method comprising administering to the subject in need thereof the formulated abaloparatide drug product according to any one of claims 1 to 3, at a daily dosage of about 80 µg of abaloparatide." On information and belief, patients, prescribers, and physicians will follow instructions in the ANDA Product label and will infringe at least claim 4 of the '041 patent. By submitting an ANDA with a label that, on information and belief, is the same as the Tymlos® (abaloparatide) label, Defendant is knowingly inducing third parties to infringe at least claim 4 of the '041 patent. By filing an ANDA, Defendant has committed an act of infringement pursuant to 35 U.S.C. § 271(e)(2)(A). Therefore, on information and belief, Defendant knowingly infringes, induces others to infringe, and/or contributes to third-party infringement of at least claim 4 of the '041 patent.

ANSWER:

Orbicular admits that the '041 patent and Orbicular's ANDA are documents that speak for themselves. Orbicular denies it infringed any valid claim of the '041 patent. Orbicular denies it infringes, induces others to infringe, and/or contributes to third-party infringement of any claim of the '041 patent. Orbicular denies the remaining allegations in Paragraph 154 of the Second Amended Complaint.

155. Upon information and belief, Defendant will commercially manufacture, use, offer to sell, and/or sell within the United States, and/or import into the United States the ANDA Product if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 155 of the Second Amended Complaint.

156. Upon information and belief, Defendant will instruct, e.g., patients, prescribers, and healthcare providers to use the ANDA Product in accordance with the proposed product labeling if ANDA No. 217245 ever receives final FDA approval.

ANSWER:

Orbicular admits it filed Orbicular's ANDA with the FDA seeking approval for the matters described therein and that Orbicular's ANDA is a document that speaks for itself. Orbicular denies the remaining allegations in Paragraph 156 of the Second Amended Complaint.

157. Upon information and belief, Defendant's commercial manufacture, use, offering to sell and/or sale within the United States, and/or importation into the United States of the ANDA Product would infringe, directly and/or indirectly, one or more of the '041 patent claims under 35 U.S.C. § 271.

ANSWER:

Denied.

158. Upon information and belief, by commercially offering for sale and/or selling the ANDA Product in accordance with its label, Defendant would knowingly induce and/or contribute to third-party infringement of one or more claims of the '041 patent under 35 U.S.C. § 271.

ANSWER:

Denied.

159. Upon information and belief, Defendant had knowledge of the '041 patent, which is a continuation of the '208 patent, prior to its issuance and is knowingly infringing the '041 patent.

ANSWER:

Orbicular denies it had knowledge of the '041 patent prior to its issuance. Orbicular denies it is infringing the '041 patent, knowingly or otherwise. Orbicular denies the remaining allegations in Paragraph 159 of the Second Amended Complaint.

160. Upon information and belief, Defendant's statements of the factual and legal bases for its opinion regarding the non-infringement of the '041 patent contained in Defendant's supplemental Notice Letter will be devoid of any objective good-faith basis in either the facts or the law.

ANSWER:

Denied.

161. Upon information and belief, Defendant will act without a reasonable basis for believing that it would not be liable for infringing the '041 patent, actively inducing infringement of the '041 patent, and/or contributing to infringement by others of the '041 patent.

ANSWER:

Denied.

162. This case therefore is "exceptional," and Radius is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

ANSWER:

Denied.

163. The acts of infringement of the '041 patent set forth above will cause Radius to suffer irreparable harm for which there is no adequate remedy at law, unless Defendant is preliminarily and permanently enjoined by this Court.

ANSWER:

Denied.

164. Radius is entitled to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an Order of this Court that the effective date of the FDA's final approval of ANDA No. 217245 be a date that is not earlier than the expiration date of the '041 patent, or any later expiration of exclusivity for the '041 patent to which Radius is or may become entitled.

ANSWER:

Denied.

GENERAL DENIAL

Defendant denies each allegation of the Second Amended Complaint not expressly admitted.

DEFENDANT'S RESPONSE TO PLAINTIFFS' PRAYER FOR RELIEF

Defendant denies that Plaintiffs are entitled to any relief sought in Plaintiffs' Prayer for Relief.

DEFENDANT'S SEPARATE DEFENSES

Without prejudice to the admissions and denials set forth in its Answer to the Second Amended Complaint, and without admitting any allegations of the Second Amended Complaint not expressly admitted, Orbicular asserts the following separate defenses to the Second Amended Complaint without assuming the burden of proof on any such defense that would otherwise rest with Plaintiffs.

FIRST SEPARATE DEFENSE
(Non-infringement of the '444 Patent)

Orbicular has not infringed, is not infringing and will not infringe any valid claim of the '444 patent.

SECOND SEPARATE DEFENSE
(Invalidity of the '444 Patent)

Each and every claim of the '444 patent is invalid for failure to comply with at least 35 U.S.C. §§ 101, 102, 103 and/or 112.

THIRD SEPARATE DEFENSE
(Non-infringement of the '333 Patent)

Orbicular has not infringed, is not infringing and will not infringe any valid claim of the '333 patent.

FOURTH SEPARATE DEFENSE
(Invalidity of the '333 Patent)

Each and every claim of the '333 patent is invalid for failure to comply with at least 35 U.S.C. §§ 101, 102, 103 and/or 112.

FIFTH SEPARATE DEFENSE
(Non-infringement of the '382 Patent)

Orbicular has not infringed, is not infringing and will not infringe will not infringe any valid claim of the '382 patent.

SIXTH SEPARATE DEFENSE
(Invalidity of the '382 Patent)

Each and every claim of the '382 patent is invalid for failure to comply with at least 35 U.S.C. §§ 101, 102, 103 and/or 112.

SEVENTH SEPARATE DEFENSE
(Non-infringement of the '208 Patent)

Orbicular has not infringed, is not infringing and will not infringe any valid claim of the '208 patent.

EIGHTH SEPARATE DEFENSE
(Invalidity of the '208 Patent)

Each and every claim of the '208 patent is invalid for failure to comply with at least 35 U.S.C. §§ 101, 102, 103 and/or 112.

NINTH SEPARATE DEFENSE
(Non-infringement of the '041 Patent)

Orbicular has not infringed, is not infringing and will not infringe any valid claim of the '041 patent.

TENTH SEPARATE DEFENSE
(Invalidity of the '041 Patent)

Each and every claim of the '041 patent is invalid for failure to comply with at least 35 U.S.C. §§ 101, 102, 103 and/or 112.

ELEVENTH SEPARATE DEFENSE
(Failure to State a Claim)

The Second Amended Complaint, in whole or in part, fails to state a claim upon which relief can be granted.

TWELVETH SEPARATE DEFENSE
(Additional Defenses)

Orbicular reserves the right to present any additional defenses or counterclaims that discovery may reveal.

DEFENDANT'S PRAYER FOR RELIEF

Orbicular respectfully requests that this Court enter judgment in its favor and against Plaintiffs as follows:

A. Dismissing the Second Amended Complaint with prejudice, denying each and every request for relief in Items (A) to (L) of Plaintiffs' Prayer for Relief, and that Plaintiffs take nothing thereby;

B. Finding that each and every claim of the '444, '333, '382, '208 and '041 patents is invalid;

C. Finding that each and every claim of the '444, '333, '382, '208 and '041 patents was not, is not and will not be infringed by Orbicular;

D. Declaring that Plaintiffs are not entitled to any injunctive remedy for any of the '444, '333, '382, '208 and '041 patents;

E. Awarding Orbicular its costs and expenses in this action;

F. Declaring that this case is exceptional under 35 U.S.C. § 285, and awarding to Orbicular its reasonable attorneys' fees; and

G. Awarding to Orbicular such further relief this Court may deem just, proper, or equitable.

Dated: November 16, 2023

Respectfully submitted,

ORBICULAR PHARMACEUTICAL TECHNOLOGIES PRIVATE LIMITED,
By and through its attorneys,

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CERTIFICATE OF SERVICE

I hereby certify that the foregoing document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing.

s/*Catherine Rajwani*
Catherine Rajwani