

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

PACIRA PHARMACEUTICALS, INC., and
PACIRA BIOSCIENCES, INC.

Plaintiffs

v.

eVenus PHARMACEUTICALS
LABORATORIES INC. and JIANGSU
HENGRUI MEDICINE CO. LTD., a Chinese
Pharmaceutical Co., and FRESENIUS KABI
USA, LLC,

Defendants.

Civil Action No.

**COMPLAINT FOR INFRINGEMENT OF
U.S. PATENT NO. 11,426,348**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Pacira Pharmaceuticals, Inc., and Pacira Biosciences, Inc. (“Plaintiffs” or “Pacira”) bring this Hatch-Waxman patent infringement suit against Defendants eVenus Pharmaceuticals Laboratories Inc. (“eVenus”), Jiangsu Hengrui Medicine Co. Ltd. (“Jiangsu Hengrui”), and Fresenius Kabi USA, LLC (“Fresenius Kabi”) (collectively, “Defendants”). Pacira alleges as follows:

CASE OVERVIEW

1. Pacira filed a Hatch-Waxman patent infringement suit against defendants eVenus and Jiangsu Hengrui in this Court on November 8, 2021 alleging infringement of U.S. Patent No. 11,033,495 (“the ‘495 patent”).¹ That First Action arose out of eVenus’s submission of an Abbreviated New Drug Application (“ANDA”) to the FDA seeking approval to commercially

¹ *Pacira Pharmaceuticals, Inc. v. eVenus Laboratories, Inc.*, No. 2:21-cv-19829-MCA-JRA (hereinafter, “The First Action”).

manufacture, use, offer for sale, sell and/or import a purported generic version of EXPAREL® bupivacaine liposome injectable suspension, 266 mg/20 mL (13.3 mg/mL) approved in NDA No. 022496, and Plaintiffs’ receipt of a Notification of Paragraph IV Certification from eVenus on the ’495 patent (“the September eVenus Notice Letter”).

2. After Plaintiffs filed the First Action, they received a second Notification of Paragraph IV Certification from eVenus on or around December 28, 2021 (“the December eVenus Notice Letter”), this time disclosing that the ANDA had been amended to seek approval to commercially manufacture, use, offer for sale, sell and/or import purported generic versions of both the 266 mg/20 mL version and 133 mg/10 mL version of EXPAREL® bupivacaine liposome injectable suspension, approved in NDA No. 022496, and certifying as to both the ’495 patent and U.S. Patent No. 11,179,336 (“the ’336 patent”). Ex. C (December eVenus Notice Letter). On February 10, 2022, Plaintiffs filed a second patent lawsuit asserting both the ’495 patent and the ’336 patent against defendants eVenus and Jiangsu Hengrui.² Plaintiffs subsequently amended the complaints in both the First and Second Actions to add defendant Fresenius Kabi. On May 9, 2022, the Court granted the parties’ request to consolidate the First and Second Actions for all purposes.³ Fact discovery in the consolidated cases remains open and is still in relatively early stages; no fact depositions have occurred. The Court held a Markman hearing on March 9, 2023, but has not yet issued a claim construction order. The thirty-month stay expires April 1, 2024 for the 266 mg/20 mL ANDA product and July 1, 2024 for the 133 mg/10 mL ANDA product.

3. On or around April 17, 2023 Defendants served a Notification of Paragraph IV Certification (“the April eVenus Notice Letter”) regarding, *inter alia*, U.S. Patent No. 11,426,348

² *Pacira Pharmaceuticals, Inc. v. eVenus Laboratories, Inc.*, No. 2:22-cv-00718 (hereinafter “the Second Action”).

³ The First Action, ECF No. 85

(“the ’348 patent”), which issued on August 30, 2022 and was listed in the FDA’s Orange Book in connection with EXPAREL® since September 2, 2022. Ex. D (April eVenus Notice Letter). The ’348 patent shares a specification with the ’495 and ’336 patents, and like the ’336 patent, claims priority to the application from which the ’495 patent issued. And like the ’495 and ’336 patents, the ’348 patent is directed to the scaled-up manufacture of EXPAREL®.

4. Defendants’ primary non-infringement argument as set forth in the December eVenus Notice Letter for the ’336 patent is that eVenus’s Proposed ANDA Products do not meet the limitation “wherein the plurality of internal aqueous chambers of the MVLs has a pH of about 5.5.” Ex. C (December eVenus Notice Letter) at 22. Independent claim 1 of the ’348 patent does not recite a similar limitation. Ex. A (the ’348 Patent) at cl. 1. Defendants’ primary non-infringement argument as set forth in the September and December eVenus Notice Letters for the ’495 patent relates to certain mixing speeds used for manufacturing the EXPAREL® compositions. Ex. C (December eVenus Notice Letter) at 21. Independent claim 1 of the ’348 patent does not recite a limitation for mixing speeds. Ex. A (the ’348 Patent) at cl. 1.

5. On the very same day—April 17—the parties met and conferred regarding whether Defendants would oppose a motion from Pacira to file a second amended complaint to assert the ’348 patent. Following the meet and confer, at Defendants’ request, Pacira shared in writing its position on a number of issues: 1) Pacira stated that, in its view, none of the ’348 patent terms required claim construction; 2) Pacira proposed a schedule to complete exchange of contentions by June 16; 3) Pacira agreed to assert no more than 15 claims from the ’348 patent; 4) Pacira agreed not to add any other patents to the case; and 5) Pacira promised to continue to meet and confer to amend the overcall case schedule as necessary.

6. In response, Defendants requested Pacira give Defendants a covenant not to sue on the remainder of Pacira's patent portfolio covering EXPAREL®, including those patents not yet issued. Defendants further requested that Pacira agree to reverse the order of the Court's Local Rules concerning contention exchanges so that Pacira would serve infringement contentions before Defendants served non-infringement and invalidity contentions. Finally, Defendants requested Pacira identify its understanding of the English word "consistently" that appears in the '348 patent claims.

7. On April 24th, Pacira sent Defendants a draft second amended complaint. Pacira declined to give a covenant not to sue and reiterated its previously-expressed view that the English word "consistently" does not require claim construction proceedings. As for exchanging contentions, Pacira offered to provide an identification of asserted claims within two business days of Defendants' written consent to amendment, which would provide about an extra week for Defendants to prepare invalidity and noninfringement contentions. Pacira also offered to entertain an alternative schedule.

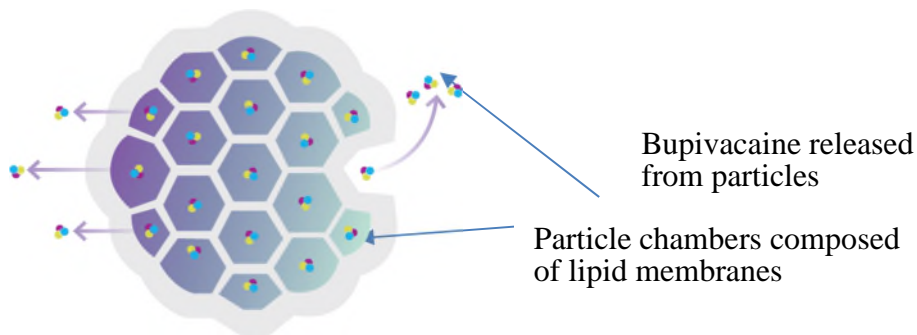
8. On April 26th, without inviting further discussion or identifying the issue that it viewed as insurmountable, Defendants notified Pacira that it would oppose a second amended complaint to add the '348 patent.

9. Pacira now files the instant complaint asserting the '348 patent.

10. The instant suit shares common issues of fact and law with the consolidated First and Second Actions. And because consolidating the instant suit with the consolidated First and Second Actions will further judicial economy and save the parties, and the Court, considerable time and expense associated with parallel litigation, Pacira intends to file a motion to consolidate along with a proposed schedule that will minimize any potential risk of prejudice to Defendants.

* * * * *

11. Like the patents asserted in the original Complaint and First Amended Complaint, the '348 patent is directed to Pacira's scaled-up manufacturing process for EXPAREL®. EXPAREL® is not a pill, nor a simple drug-containing solution. Rather, EXPAREL® is an injectable suspension, consisting of millions of microscopic, spherical particles, called multivesicular liposomes (MVLs). Each MVL particle comprises tens of thousands of chambers which contain the drug (bupivacaine). Following administration to a patient, the particle chambers begin to release drug slowly, through a complex rearrangement process, over a period of days. Shown below is a cross-sectional diagram of an MVL, showing how each individual vesicle contains and releases bupivacaine:



12. The manufacturing process required to form the MVLs that comprise EXPAREL® is very complex and involves multiple emulsion steps that must be performed under precisely controlled conditions. Two of the process conditions of utmost importance are pH and timing.

13. First, the manufacturing process and the product itself are highly sensitive to pH. Inadequate pH control can cause process failure. Unfortunately, multiple steps in the process for making bupivacaine MVLs must be performed at pH extremes, and multiple components being used in the process (including bupivacaine itself) must themselves be utilized at pH extremes—and those pH extremes often differ. As one example, during particle formation, the internal pH of

the bupivacaine solution is very low, while the external pH is very high. Bupivacaine is highly prone to crystallization if exposed to even slightly elevated pH. Thus, if during mixing, the bupivacaine is exposed to the high-pH external environment, it can crystallize, disrupt particle formation, and result in batch failure. Further, following successful manufacture of a batch of EXPAREL®, the pH must still be tightly controlled. The pH of the final product MVL particles must be maintained in a narrow range that is adequately acidic to ensure that the bupivacaine stays dissolved inside the particle, but not so acidic that it promotes acid-catalyzed membrane degradation.

14. Second, the timing of the water-oil-water emulsification steps is critical. You only have about sixty seconds to complete the crucial, yet highly sensitive, “second emulsion” step—the mixing step during which the MVLs are formed. During the second emulsion, the lipid membranes contain solvent and are very fluid and vulnerable to disruption, potentially exposing the bupivacaine to high pH that may cause it to crystallize and destroy particles (as described above). The mixing time limit is thus virtually the same regardless of batch size—whether a few mL on a lab bench, or a 200 liter commercial batch. The bigger the batch, the more time and mixing energy is required to emulsify the components. The challenge of the second emulsification step timing was considered by Pacira scientists to be potentially insurmountable. Pacira engineers were so skeptical that developing a 200L batch process would be possible, that they invested several years into the development of an alternative “spray” processing approach (which ultimately failed) before attempting development of a 200L batch process.

15. But out of these challenges—solved through approximately 7 years of experimentation and tens of millions of development dollars—Pacira discovered unexpected advantages of the EXPAREL® resulting from this scaled-up process. For example, the second

emulsion step done in a larger scale unexpectedly led to a wider MVL particle size distribution, along with unexpectedly higher internal lysine concentration and pH. And while common manufacturing wisdom suggests that a narrow particle size distribution is preferred and that lysine encapsulation should be avoided, these batches nonetheless demonstrate better stability than those from Pacira's prior process, showing lower levels of lipid degradation products (e.g., erucic acid) after 6 months at 25 degrees Celsius.

NATURE OF ACTION

16. This is an action for patent infringement under the patent laws of the United States, 35 U.S.C. § 100, et seq., including 35 U.S.C. § 271(e)(2), the Drug Price Competition and Patent Term Restoration Act of 1984; 21 U.S.C. § 355(j) (the "Hatch-Waxman Act"); 35 U.S.C. § 271(a)-(c); and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, that arises out of Defendants' submission of an ANDA to the FDA seeking approval to commercially manufacture, use, offer for sale, sell and/or import proposed generic versions of EXPAREL® (bupivacaine liposome injectable suspension, 133 mg/10 mL and 266 mg/20 mL (13.3 mg/mL))⁴ prior to the expiration of the '348 patent. Plaintiffs seek injunctive relief precluding infringement, attorneys' fees, and any other relief the Court deems just and proper.

PARTIES

17. Plaintiff Pacira Pharmaceuticals, Inc. is a corporation organized and existing under the laws of California with its principal place of business at 5401 West Kennedy Blvd, Lincoln Center Suite 890. Tampa, FL.

⁴ Hereinafter, "eVenus's Proposed ANDA Products."

18. Plaintiff Pacira BioSciences, Inc. is a corporation organized and existing under the laws of Delaware with its principal place of business at 5401 West Kennedy Blvd, Lincoln Center Suite 890. Tampa, FL.

19. Defendant eVenus Pharmaceuticals Laboratories Inc. is a corporation organized and existing under the laws of the State of New Jersey, having a principal place of business at 506 Carnegie Center, Suite 100, Princeton, New Jersey, 08540. eVenus is in the business of selling and distributing generic drugs for the U.S. Market.

20. Defendant Jiangsu Hengrui Pharmaceuticals Co. Ltd. is a corporation organized and existing under the laws of China with its principal place of business at No. 7 Kunlunshan Road, Lianyungang Eco & Tech Development Zone, Lianyungang, Jiangsu, 222002, China. Jiangsu Hengrui is in the business of, among other things, manufacturing, marketing, selling, and distributing generic drugs for the U.S. market, including through its subsidiary eVenus. Jiangsu Hengrui is the holder of Drug Master File (“DMF”) No. 34900, bupivacaine base. On information and belief, Jiangsu Hengrui will manufacture the active pharmaceutical ingredient (“API”) for eVenus’s Proposed ANDA Products.

21. Defendant Fresenius Kabi USA, LLC is a limited liability corporation organized and existing under the laws of Delaware, with a principal place of business at Three Corporate Drive, Lake Zurich, Illinois 60047. Fresenius Kabi is in the business of manufacturing, marketing, and selling generic drugs for the U.S. market. On information and belief, Fresenius Kabi is licensed to commercialize the eVenus’s Proposed ANDA Products in the United States, including in the State of New Jersey, in the event FDA approves the eVenus ANDA.

JURISDICTION AND VENUE

Subject Matter Jurisdiction

22. This action arises under the patent laws of the United States of America, United States Code, Title 35, Section 1, *et seq.* and the Declaratory Judgment Act.

23. This Court has subject matter jurisdiction over the action under 28 U.S.C. §§ 1331, 1338, 2201, and 2202.

24. This Court can provide the relief sought in this Declaratory Judgment counts of this Complaint because an actual case and controversy exists between the parties within the scope of this Court's jurisdiction pursuant to 28 U.S.C. § 2201, at least because Plaintiffs have already sued Defendants for infringing two related patents on the same drug product.

Personal Jurisdiction and Venue

25. This Court has personal jurisdiction over eVenus because eVenus is incorporated in New Jersey and has its primary place of business in New Jersey, at 506 Carnegie Center, Suite 100, Princeton, New Jersey, 08540.

26. eVenus is also subject to personal jurisdiction in New Jersey because, among other things, eVenus, itself and through its affiliates, has purposely availed itself of the benefits and protections of New Jersey's laws such that it should reasonably anticipate being sued in this Court.

27. eVenus, itself and through its affiliates, develops, manufactures, imports, markets, distributes, uses, offers to sell, and/or sells generic drugs throughout the United States, including in the State of New Jersey, and therefore transacts business within the State of New Jersey related to Pacira's claims, and/or has engaged in systematic and continuous business contacts within the State of New Jersey.

28. eVenus is registered as wholesaler with the State of New Jersey's Department of Health under Registration No. 5004028. On information and belief, eVenus, itself and through its

affiliates, will use this license to offer for sale and to sell eVenus's Proposed ANDA Products throughout the United States, including New Jersey.

29. eVenus is registered with the State of New Jersey's Division of Revenue and Enterprise Services as a business operating in New Jersey under Business ID No. 0400276509.

30. Venue is proper in this Court pursuant to 28 U.S.C. § 1400(b) as to eVenus because, on information and belief, eVenus has a regular and established place of business in New Jersey, and because, on information and belief, eVenus has committed or aided, abetted, contributed to, and/or participated in the commission of, acts of infringement of the asserted patent that will lead to foreseeable harm and injury to Pacira by preparing or assisting in preparing eVenus's ANDA in New Jersey and/or with the intention of seeking to market eVenus's Proposed ANDA Products nationwide, including within New Jersey.

31. On information and belief, Jiangsu Hengrui is subject to personal jurisdiction in New Jersey because, among other things, Jiangsu Hengrui itself and through its wholly owned subsidiary, eVenus, has purposefully availed itself of the benefits and protections of New Jersey's laws such that it should reasonably anticipate being sued in this Court.

32. On information and belief, Jiangsu Hengrui, itself and through its affiliates, develops, manufactures, imports, markets, distributes, uses, offers to sell, and/or sells generic drugs throughout the United States, including in the State of New Jersey, and therefore transacts business within the State of New Jersey related to Pacira's claims, and/or has engaged in systematic and continuous business with contacts within the State of New Jersey.

33. On information and belief, Jiangsu Hengrui is subject to personal jurisdiction in New Jersey because it directs and controls eVenus and therefore the activities of eVenus in this jurisdiction are attributed to Jiangsu Hengrui. Moreover, Jiangsu Hengrui, through its wholly

owned subsidiary eVenus, has a regular and established place of business in New Jersey. On information and belief, Jiangsu Hengrui has been and is engaging in activities directed toward infringement of the patent-in-suit by, among other things, preparing and submitting the Jiangsu Hengrui DMF, and acting in concert with eVenus in the preparation and submission of eVenus's ANDA seeking FDA approval to market eVenus's Proposed ANDA Products throughout the United States, including New Jersey, before expiration of the '348 patent. On information and belief, Jiangsu Hengrui will manufacture the API for eVenus's Proposed ANDA Products.

34. On information and belief, Jiangsu Hengrui and eVenus operate and act, and will continue to operate and act, in concert as an integrated, unitary business with respect to eVenus's Proposed ANDA Products. Jiangsu Hengrui and eVenus work in concert with respect to the manufacturing, marketing, sale, and distribution of generic pharmaceutical products throughout the United States, including New Jersey.

35. On information and belief, eVenus acts at the direction, and for the benefit, of Jiangsu Hengrui, and is controlled by Jiangsu Hengrui.

36. Jiangsu Hengrui consented to jurisdiction in New Jersey in at least one prior case arising out of the filing of an ANDA. *See Janssen Prods., L.P. v. eVenus Pharma. Labs. Inc.*, No. 20-cv-9369 (D.N.J.). Moreover, Jiangsu Hengrui did not challenge personal jurisdiction in the First Action or Second Action.

37. Venue is proper in this district for Jiangsu Hengrui pursuant to 28 U.S.C. §§ 1391(c) and/or 1400(b) because Jiangsu Hengrui is a company organized and existing under the laws of China and may be sued in any judicial district.

38. In the alternative, as to Jiangsu Hengrui, this Court's exercise of personal jurisdiction is proper pursuant to Fed. R. Civ. P. 4. On information and belief, Jiangsu is a foreign

company organized and existing under the laws of China, with a principal place of business in Lianyungang, Jiangsu, China.

39. This Court has personal jurisdiction over Jiangsu Hengrui because the requirements of Fed. R. Civ. P. 4(k)(2)(A) are met. First, Plaintiffs' claims arise under federal law. Second, Jiangsu Hengrui is a foreign defendant that is not subject to jurisdiction in any state's courts of general jurisdiction. Third, Jiangsu Hengrui has sufficient contacts with the United States, including, for example, on information and belief, participating in the preparation and submission of eVenus's ANDA, preparing and submitting the Jiangsu Hengrui DMF to FDA, and/or manufacturing and/or selling pharmaceutical products distributed throughout the United States, including in this judicial district, such that this Court's exercise of jurisdiction over Jiangsu Hengrui satisfies due process.

40. Litigation in the District of New Jersey would not unduly burden Jiangsu Hengrui. The United States has a substantial interest in adjudicating the dispute and enforcing its patent laws and Plaintiffs have a substantial interest in obtaining convenient and effective relief for violations of their property interests. Also, the States have a shared interest in the substantive policy of the intellectual property laws of the United States.

41. This Court has personal jurisdiction over Fresenius Kabi because on information and belief Fresenius Kabi has purposely availed itself of the benefits and protections of New Jersey's laws such that it should reasonably anticipate being haled into court here.

42. This Court has personal jurisdiction over Fresenius Kabi because, *inter alia*, it: (1) has purposefully availed itself of the privilege of doing business in the State of New Jersey; (2) intends to import, market, sell and/or distribute the eVenus's Proposed ANDA Products to residents of New Jersey; (3) has continuous and systematic contacts with the State of New Jersey

and regularly conducts business in the State of New Jersey, either directly or through one or more of its affiliates, agents, and/or alter egos; (4) makes its generic pharmaceutical products available in New Jersey; (5) maintains a broad distributorship network within New Jersey; and (6) enjoys substantial income from sales of its generic pharmaceutical products in New Jersey.

43. On information and belief, Fresenius Kabi is registered to do business in New Jersey under Entity Identification No. 0600313148.

44. On information and belief, Fresenius Kabi is registered with the State of New Jersey's Department of Health as a wholesaler under Registration No. 5003710.

45. On information and belief, Fresenius Kabi has had persistent and continuous contacts with this judicial district, including developing and marketing pharmaceutical products that are sold in this judicial district and selling pharmaceutical products in this judicial district.

46. On information and belief, Fresenius Kabi directly and/or through one or more of its affiliates, agents, and/or alter egos, distributes, and sells generic pharmaceutical products throughout the United States, including in this judicial district.

47. On information and belief, Fresenius Kabi derives substantial revenue from selling generic pharmaceutical products throughout the United States, including in this judicial district.

48. On information and belief, Fresenius Kabi directly and/or through one or more of its affiliates, agents, and/or alter egos has an extensive network of physicians, medical facilities, wholesalers, and distributors in this judicial district.

49. On information and belief Fresenius Kabi has been and is engaging in activities directed toward infringement of the patent-in-suit, including by acting in concert with eVenus and Jiangsu Hengrui with respect to the development, regulatory approval, commercial manufacture, marketing, sale, offer for sale, and/or distribution of eVenus's Proposed ANDA Products before

expiration of the '348 patent. On information and belief, Fresenius Kabi intends to engage in importing, marketing, selling, distributing and/or using eVenus's Proposed ANDA Products before expiration of the '348 patent throughout the United States, including in New Jersey.

50. On information and belief, Fresenius Kabi intends to take advantage of its established channels of distribution in New Jersey for the sale of eVenus's Proposed ANDA Products.

51. On information and belief, eVenus and Jiangsu act for the benefit of Fresenius Kabi with respect to eVenus's Proposed ANDA Products.

52. On information and belief, Fresenius Kabi has a regular and established place of business in New Jersey. For instance, at least one Fresenius Kabi employee has a LinkedIn page identifying a Fresenius Kabi business location in New Jersey.

53. On information and belief, the regular and established place of business in New Jersey of eVenus and the infringing acts in New Jersey by eVenus are imputable to Fresenius Kabi and Jiangsu Hengrui because that location and those acts were instrumental in furtherance of a partnership among the Defendants to obtain FDA approval to market, and subsequently to commercialize, the eVenus's Proposed ANDA Products.

54. On information and belief, Fresenius Kabi knows and intends that eVenus's Proposed ANDA Products will be distributed and sold in New Jersey and will thereby displace sales of EXPAREL®, 133 mg/10 mL and 266 mg/20 mL (13.1 mg/mL), causing injury to Plaintiffs.

55. Venue is proper in this district for Fresenius Kabi pursuant to 28 U.S.C. § 1400(b).

THE EXPAREL[®] DRUG PRODUCT

56. Pacira Pharmaceuticals, Inc. is the holder of the New Drug Application (“NDA”) No. 022496, under which the FDA approved the commercial marketing of EXPAREL[®] (bupivacaine liposome injectable suspension) in two different dosage forms—266 mg/20 mL and 133 mg/10 mL (both 13.3 mg/mL)—on October 28, 2011, under Section 505(a) of the Federal Food, Drug, and Cosmetic Act (“FDCA”), 21 U.S.C. § 355(a). EXPAREL[®] is currently approved in patients 6 years of age and older for single dose infiltration into the surgical site to produce postsurgical analgesia, and in adults as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Pacira distributes EXPAREL[®] in the United States in a 266 mg/20 mL (13.3 mg/mL) strength single-dose vial and a 133 mg/10 mL (13.3 mg/mL) strength single dose vial. A true and correct copy of the current prescribing information for EXPAREL[®] is attached as Exhibit B.

57. EXPAREL[®] is a first-of-its-kind, single dose local anesthetic administered at the time of surgery to control pain and reduce or eliminate the use of opioids for acute postsurgical pain. The active ingredient in EXPAREL[®], bupivacaine, is encapsulated in multivesicular liposomes allowing for gradual release of bupivacaine over time as the lipid membranes are absorbed, prolonging the action of bupivacaine. The administration of bupivacaine in an encapsulated multivesicular liposome at the surgical site can control pain for several days following a surgery. The delivery mechanism of the drug and gradual release reduces or eliminates the use of highly addictive opioids for acute postsurgical pain. The delivery system also eliminates the need for catheters or pumps, decreasing cost. Because of at least these unique features, EXPAREL[®] has been viewed as a significant advance in the field of anesthesiology.

THE PATENT-IN-SUIT

58. The '348 patent, entitled "Manufacturing of Bupivacaine Multivesicular Liposomes," was duly and legally issued on August 30, 2022, and names Jeffrey S. Hall, David J. Turnbull, John J. Grigsby, Jr., Soroush M. Ardekani, and Kathleen D. A. Los as the inventors. Attached as Exhibit A is a true and correct copy of the '348 patent.

59. Pacira Pharmaceuticals, Inc. is the owner and assignee of the '348 patent and has the right to enforce the '348 patent.

60. Since September 2, 2022 the '348 patent has been listed in the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book," which provides notice concerning patents covering FDA-approved drugs.

61. The Orange Book lists the expiration of the '348 patent as January 22, 2041.

62. The '348 patent is directed to compositions of bupivacaine encapsulated multivesicular liposomes (MVLs) with enhanced stability that unexpectedly resulted from new and improved commercial scale manufacturing processes for making bupivacaine encapsulated multivesicular liposomes (MVLs). The newly developed processes provide up to 5-fold increase in final product volume as compared to the prior methods for the manufacturing of EXPAREL®. Representative claims 2 and 41 (and claim 1 from which claim 2 depends) are reproduced below:

1. Batches comprising compositions of bupivacaine multivesicular liposomes (MVLs), comprising:
 - (a) bupivacaine residing inside a plurality of internal aqueous chambers of the MVLS separated by lipid membranes, wherein the lipid membranes comprise 1,2-dierucoylphosphadtidylcholine (DEPC), 1, 2-dipalmitoyl-sn-glycero-3 phospho-rac-(1-glycerol) (DPPG), and at least one neutral lipid;
 - (b) and an aqueous medium in which the bupivacaine encapsulated MVLs are suspended;

- (c) wherein the batches consistently comprise an erucic acid concentration of less than about 109 $\mu\text{g}/\text{mL}$ after the compositions are stored at 25°C for six months.
- 2. The batches of claim 1, wherein the batches comprise the erucic acid concentration of about 99 $\mu\text{g}/\text{mL}$ or less after the compositions are stored at 25 ° C for six months.
- 41. The batches of claim 2, wherein the internal aqueous chambers of the MVLs comprise lysine, and the encapsulated lysine concentration in the bupivacaine encapsulated MVLs compositions is about 0.03 mg/mL.

63. On information and belief, upon approval of eVenus’s ANDA, Defendants’ conduct will satisfy the preamble and limitations (a), (b) of claim 1 by making **“batches comprising compositions of bupivacaine multivesicular liposomes (MVLs) comprising bupivacaine residing inside a plurality of internal aqueous chambers of the MVLs separated by lipid membranes, wherein the lipid membranes comprise 1,2-dierucoylphosphadtidylcholine (DEPC), 1, 2-dipalmitoyl-sn-glycero-3phospho-rac-(1-glycerol) (DPPG), and at least one neutral lipid and an aqueous medium in which the bupivacaine encapsulated MVLs are suspended.”** On information and belief, for eVenus to obtain FDA approval of the eVenus’s Proposed ANDA Products, Defendants must prove that the eVenus’s Proposed ANDA Products are bioequivalent to EXPAREL®. For example, the December eVenus Notice Letter stated that the eVenus ANDA contains “any required bioavailability and/or bioequivalence data or information in order to obtain approval to engage in the commercial, manufacture, use or sale of bupivacaine liposome injectable suspension.” Ex. C (December eVenus Notice Letter) at 2. On information and belief, eVenus’s Proposed ANDA Products must satisfy the preamble and limitations (a), (b) of claim 1 for eVenus’s Proposed ANDA Products to be considered bioequivalent to EXPAREL®. The ’336 and ’495 patents asserted in the First and Second Actions recite similar limitations to the preamble and limitations

(a), (b) of claim 1 of the '348 patent. Tellingly, in the December eVenus Notice Letter, Defendants do not dispute that the eVenus's Proposed ANDA Products satisfy those limitations.

64. On information and belief, eVenus's Proposed ANDA Products will satisfy the limitation in claim 2 "**wherein the batches consistently comprise an erucic acid concentration of less than about 99 µg/mL after the compositions are stored at 25°C for six months.**" Erucic acid is a degradation product that accumulates as the DEPC hydrolyzes and is a stability marker. The more erucic acid, the more degradation has occurred. FDA required Pacira to submit stability data for EXPAREL® batches stored at 25°C for six months to simulate the product characteristics at the end of a two-year shelf life stored at room temperature. One of the unexpected properties of the claimed batches manufactured in 200 L batch sizes is that the compositions have less erucic acid after being stored at 25°C for six months than 45 L batches. On information and belief, the eVenus's Proposed ANDA Products will consistently comprise an erucic acid concentration of less than about 99 µg/mL after the compositions are stored at 25°C for six months. Claim 7 of the '495 patent and claim 7 of the '336 patent asserted in the First and Second Actions recite "wherein the erucic acid concentration in the composition is about 99 µg/mL or less after the composition is stored at 25° C for six months." In the December eVenus Notice Letter, Defendants did not dispute that eVenus's Proposed ANDA Products satisfy the limitation. *See* Ex. C (December eVenus Notice Letter) at 21-22.

65. On information and belief, eVenus's Proposed ANDA Products will infringe claim 41 which depends from claim 2 and additionally requires: "**wherein the internal aqueous chambers of the MVLs comprise lysine, and the encapsulated lysine concentration in the bupivacaine encapsulated MVLs compositions is about 0.03 mg/mL.**" Pacira's scaled-up manufacturing process for EXPAREL® surprisingly yielded MVL compositions with higher

concentrations of internal lysine. Conventional wisdom teaches that it's desirable to have the lysine restricted to the aqueous solution outside the MVL particles to facilitate MVL particle formation during the second emulsion step. Due to inefficiencies in mixing large volumes during the second emulsion step, an unexpectedly higher amount of lysine becomes trapped inside the MVLs conferring unexpected stability benefits. Claim 10 of the '336 patent asserted in the Second Action recites "wherein the encapsulated lysine concentration in the bupivacaine encapsulated MVLs composition is about 0.030 mg/mL to about 0.032 mg/mL." In the December eVenus Notice Letter, Defendants did not dispute that eVenus's Proposed ANDA Products satisfy the limitation for encapsulated lysine concentration in the bupivacaine encapsulated MVLs composition that is about 0.030 mg/mL to about 0.032 mg/mL.

66. The '348 patent also claims methods for treating or ameliorating pain through the administration of the improved compositions of bupivacaine encapsulated multivesicular liposomes (MVLs) embodied by EXPAREL[®]. Claim 21, which depends from claim 19, is representative of the method claims. Both claims are reproduced below:

1. A method of treating or ameliorating pain in a subject in need thereof, comprising administering a composition of claim 1 to the subject.
2. The method of claim 19, wherein the composition has a pH of about 6.5 after the composition is stored at 25°C for six months.

67. As explained below, Defendants will include within the packaging of eVenus's Proposed ANDA Products, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to infringe at least claims 19 and 21.

DEFENDANTS' SUBMISSION OF eVENUS'S ANDA

68. On information and belief, Defendants have submitted or caused the submission of eVenus's ANDA No. 214348 to the FDA under 21 U.S.C. § 355(j), to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of eVenus's Proposed ANDA Products, a purported generic version of EXPAREL®, prior to the expiration of the '348 patent.

69. eVenus served the April eVenus Notice Letter notifying Pacira of the submission of eVenus's ANDA to the FDA to obtain approval under the FDCA to engage in the commercial manufacture, use, or sale of eVenus's Proposed ANDA Products prior to the expiration of the '348 patent.

70. In the eVenus PIV Letters, eVenus also notified Pacira that, as part of its ANDA, eVenus had filed a Paragraph IV Certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), with respect to the '348 patent.

71. On information and belief, eVenus submitted its ANDA to the FDA containing certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) asserting that the '348 patent is invalid, unenforceable, and/or will not be infringed by the manufacture, use, offer for sale, sale, and/or importation of eVenus's Proposed ANDA Products.

COUNT I

(Infringement of the '348 Patent Under 35 U.S.C. § 271(e)(2))

72. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

73. Defendants submitted ANDA No. 214348 to the FDA under section 505(j) of the FDCA to obtain approval to engage in the commercial manufacture, importation, use, sale, or offer for sale of eVenus's Proposed ANDA Products. By submitting the application, Defendants have committed an act of infringement of the '348 patent under 35 U.S.C. § 271(e)(2)(A).

74. The commercial manufacture, importation, use, sale, or offer for sale of will constitute an act of direct infringement of the '348 patent by eVenus's Proposed ANDA Products, either literally or under the doctrine of equivalents.

75. On information and belief, Defendants became aware of the '348 patent no later than when it was issued by the Patent Office and/or listed in the Orange Book as covering methods of using EXPAREL[®]. Defendants' service of the April eVenus Notice Letter reflects that Defendants had actual knowledge of the '348 patent.

76. On information and belief, Defendants knew or should have known that their commercial making, using, offering to sell, selling, importing or otherwise promoting and/or distributing of eVenus's Proposed ANDA Products, with its labeling, will actively induce the direct infringement of the '348 patent.

77. On information and belief, Defendants knew or should have known that eVenus's Proposed ANDA Products will be especially made or especially adapted for use in an infringement of the '348 patent, and are not staple articles or commodities of commerce suitable for substantial non-infringing use, as evidence by, for example, the contents of their proposed labeling. And, on information and belief, Defendants knew or should have known that its commercial offering to sell, selling, importing or otherwise distributing of eVenus's Proposed ANDA Products will actively contribute to the direct infringement of the '348 patent.

78. Unless and until Defendants are enjoined from infringing the '348 patent, Plaintiffs will suffer irreparable injury for which damages are an inadequate remedy.

79. Plaintiffs are entitled to the relief provided by 35 U.S.C. § 271(e)(4), including an order of this Court stating that the effective date of approval of Defendants' ANDA No. 214348 be a date that is not earlier than the expiration date of the '348 patent.

COUNT II

(Declaratory Judgment of Infringement of the '348 Patent Under § 271(a))

80. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

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

82. There is an actual case or controversy such that the Court may entertain Plaintiffs' request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

83. On information and belief, Defendants will engage in the commercial manufacture, use, offer for sale, sale, and/or importation of eVenus's Proposed ANDA Products immediately and imminently upon FDA approval of ANDA No. 214348.

84. Defendants' actions, including but not limited to, the development of eVenus's Proposed ANDA Products, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Defendants have made and will continue to make substantial preparation in the United States, including in the District of New Jersey, to manufacture, sell, offer to sell, and/or import eVenus's Proposed ANDA Products.

85. On information and belief, eVenus's Proposed ANDA Products practice all limitations of at least claims 2 and 41 of the '348 patent, either literally or under the doctrine of equivalents, as detailed above, and thus the manufacture, importation, use, sale, and/or offer for sale of eVenus's Proposed ANDA Products will constitute an act of infringement of the '348 patent.

86. The commercial manufacture, importation, use, sale, or offer for sale of eVenus's Proposed ANDA Products in violation of Plaintiffs' patent rights will cause harm to Plaintiffs, for which damages are inadequate.

87. Plaintiffs are entitled to a declaratory judgment that the future manufacture, use, offer for sale, sale and/or importation of eVenus's Proposed ANDA Products before patent expiration will constitute direct infringement of at least claims 2 and 41 of the '348 patent under 35 U.S.C. § 271(a).

88. Unless and until Defendants are enjoined from infringing the '348 patent, Plaintiffs will suffer irreparable injury for which damages are an inadequate remedy.

COUNT III

(Declaratory Judgment of Infringement of the '348 Patent Under 35 U.S.C. § 271(b))

89. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

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

91. There is an actual case or controversy such that the Court may entertain Plaintiffs' request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

92. Defendants' service of the April eVenus Notice Letter reflects that Defendants had actual knowledge of the '348 patent.

93. On information and belief, Defendants became aware of the '348 patent when it was issued by the Patent Office on August 30, 2022 and/or listed in the publicly available Orange Book on September 2, 2022 as covering methods of using EXPAREL®.

94. On information and belief, Defendants will engage in the commercial manufacture, use, offer for sale, sale, importation or other promotion and/or distribution of eVenus's Proposed ANDA Products immediately and imminently upon FDA approval of ANDA No. 214348.

95. Defendants' actions, including but not limited to, the development of eVenus's Proposed ANDA Products, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Defendants have made and will continue to make substantial preparation in the United

States, including in the District of New Jersey, to manufacture, sell, offer to sell, import or otherwise promote eVenus's Proposed ANDA Products.

96. On information and belief, Defendants will include within the packaging of eVenus's Proposed ANDA Products, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to perform the method of at least claims 19 and 21 of the '348 patent and use batches of compositions of bupivacaine multivesicular liposomes recited in at least claim 2 of the '348 patent.

97. On information and belief, healthcare providers treating or ameliorating a patient's pain using eVenus's Proposed ANDA Products within the United States according to the instructions in the products' labeling will directly infringe at least claims 19 and 21 of the '348 patent, either literally or under the doctrine of equivalents.

98. On information and belief, Defendants possess specific intent to encourage direct infringement of at least claims 19 and 21 of the '348 patent, including because Defendants' labeling for eVenus's Proposed ANDA Products instructs users to use the patented compositions and to perform the patented method, providing evidence of an affirmative intent to induce infringement. Furthermore, because EXPAREL[®] and eVenus's Proposed ANDA Products have no substantial non-infringing uses, Defendants intend for the use of its generic version of EXPAREL[®] to directly infringe at least claims 19 and 21 of the '348 patent.

99. On information and belief, upon awareness of the '348 patent, Defendants either actually knew of the potential for infringement of at least claims 19 and 21 of the '348 patent, or were willfully blind as to the potential for that infringement at least because Defendants provide instructions for infringement of at least claims 19 and 21 of the '348 patent in its proposed product labeling.

100. The commercial making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of eVenus's Proposed ANDA Products, with its labeling, will constitute an act of active inducement of infringement of at least claims 19 and 21 of the '348 patent.

101. The commercial making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of eVenus's Proposed ANDA Products in violation of Plaintiffs' patent rights will cause harm to Plaintiffs, for which damages are inadequate.

102. Plaintiffs are entitled to a declaratory judgment that the future making, using, offering to sell, selling, importing, or otherwise promoting and/or distributing of eVenus's Proposed ANDA Products before patent expiration will constitute active inducement of infringement of at least claims 19 and 21 of the '348 patent under 35 U.S.C. § 271(b).

103. Unless and until Defendants are enjoined from infringing the '348 patent, Plaintiffs will suffer irreparable injury for which damages are an inadequate remedy.

COUNT IV

(Declaratory Judgment of Infringement of the '348 Patent Under 35 U.S.C. § 271(c))

104. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

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

106. There is an actual case or controversy such that the Court may entertain Plaintiffs' request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

107. Defendants' service of the April eVenus Notice Letter reflects that Defendants had actual knowledge of the '348 patent.

108. On information and belief, Defendants became aware of the '348 patent when it was issued by the Patent Office on August 30, 2022 and/or listed in the publicly available Orange Book on September 2, 2022 as covering EXPAREL®.

109. On information and belief, Defendants will engage in the commercial manufacture, use, offer for sale, sale, importation and/or other distribution of eVenus's Proposed ANDA Products immediately and imminently upon FDA approval of ANDA No. 214348.

110. Defendants' actions, including but not limited to, the development of eVenus's Proposed ANDA Products, and the filing of an ANDA with a Paragraph IV Certification, reliably predict that Defendants have made and will continue to make substantial preparation in the United States, including in the District of New Jersey, to sell, offer to sell, import and/or otherwise distribute eVenus's Proposed ANDA Products.

111. On information and belief, Defendants will include within the packaging of its eVenus's Proposed ANDA Products, or will otherwise make available to healthcare providers and patients upon FDA approval, labeling that instructs healthcare providers to use the Proposed ANDA Products to perform the method of at least claims 19 and 21 of the '348 patent.

112. On information and belief, healthcare providers administering eVenus's Proposed ANDA Products to patients to treat or ameliorate pain within the United States according to the instructions in the product's labeling will directly infringe at least claims 19 and 21 of the '348 patent, either literally or under the doctrine of equivalents.

113. On information and belief, Defendants know that eVenus's Proposed ANDA Products are a material part of the method of at least claims 19 and 21 of the '348 patent, including as evidenced in the contents of its proposed label. On information and belief, eVenus's Proposed ANDA Products were especially made or especially adapted for use by a healthcare provider in a

manner that will directly infringe at least claim 19 and 21 of the '348 patent, as evidenced in the contents of its proposed labeling. On information and belief, eVenus's Proposed ANDA Products are not a staple article of commerce suitable for substantial non-infringing use, as evidenced by the contents of its proposed labeling and the fact that it seeks FDA approval for a particular use. There are no suitable uses for eVenus's Proposed ANDA Products other than treating patients pursuant to FDA's approval for such products.

114. Thus, on information and belief, Defendants will contribute to the infringement of at least claims 19 and 21 of the '348 patent in this District and elsewhere in the United States by offering to sell, selling, importing, or otherwise distributing eVenus's Proposed ANDA Products, which are material for use in practicing the method of at least claims 19 and 21 of the '348 patent.

115. The commercial offering to sell, selling, importing and/or other distribution of eVenus's Proposed ANDA Products for use and for practicing the patented method in violation of Plaintiffs' patent rights will cause harm to Plaintiffs, for which damages are inadequate.

116. Plaintiffs are entitled to a declaratory judgment that the future offer for sale, sale, importation and/or other distribution of eVenus's Proposed ANDA Products before expiration of the '348 patent will constitute contributory infringement of the claims of the '348 patent under 35 U.S.C. § 271(c).

117. Unless and until Defendants are enjoined from infringing the '348 patent, Plaintiffs will suffer irreparable injury for which damages are an inadequate remedy.

DEMAND FOR JURY TRIAL

118. Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs hereby demand a trial by jury on all issues triable to a jury. Specifically, Plaintiffs demand a jury trial in the event that there is a launch at risk and damages are in issue.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the Court to enter judgment in their favor against Defendants:

A. That judgment be issued that Defendants have infringed the '348 patent under 35 U.S.C. § 271(e)(2)(A) by submitting ANDA 214348 under section 505(j) of the Federal Food, Drug and Cosmetic Act, and that the commercial manufacture, use, offer to sell, or sale within the United States, or importation into the United States, of eVenus's Proposed ANDA Products will constitute an act of infringement of the '348 patent;

B. That an order be issued under 35 U.S.C. § 271(e)(4)(A) that the effective date of any FDA approval of Defendants' ANDA No. 214348 shall be a date which is not earlier than the expiration date of the '348 patent, as extended by any applicable period of exclusivity;

C. That an injunction be issued under 35 U.S.C. § 271(e)(4)(B) permanently enjoining Defendants, their officers, agents, servants, employees, licensees, representatives, and attorneys, and all other persons acting or attempting to act in active concert or participation with them or acting on their behalf, from engaging in the commercial manufacture, use, offer to sell, or sale within the United States, or importation into the United States, of any drug product covered by, or drug product whose use is covered by, the '348 patent;

D. That a declaration be issued under 28 U.S.C. § 2201 that the manufacture, use, offer for sale, sale and/or importation of eVenus's Proposed ANDA Products before expiration of the '348 patent does and will infringe the '348 patent.

E. That an order be issued preliminarily and permanently enjoining Defendants and their affiliates, subsidiaries, officers, agents, employees, attorneys, and all persons in active concert or participation with any of them, or acting on their behalf, from infringing the '348 patent;

F. If Defendants engage in the commercial manufacture, use, offer to sell, sale, or importation of eVenus's Proposed ANDA Products disclosed in ANDA No. 214348 prior to the expiration of the '348 patent, as extended by any applicable period of exclusivity, judgment

awarding Plaintiffs damages resulting from such infringement under 35 U.S.C. § 271(e)(4)(C), increased to treble the amount found and/or assessed together with prejudgment and post-judgment interest and costs under 35 U.S.C. § 284;

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

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

I. That this Court award such other and further relief as it may deem just and proper.

Dated: April 28, 2023

Respectfully submitted,

By: /s/ John E. Flaherty

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LOCAL RULE 11.2 CERTIFICATION

The ANDA and Defendants' Proposed ANDA Products are the subject of two patent litigations in this Court: *Pacira Pharmaceuticals, Inc. v. eVenus Laboratories, Inc.*, No. 2:21-cv-19829-MCA-JRA and *Pacira Pharmaceuticals, Inc. v. eVenus Laboratories, Inc.*, No. 2:22-cv-00718. These matters involve the same parties as the instant suit and are consolidated under No. 2:21-19829-MCA-JRA.

I certify under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

April 28, 2023.

By: John E. Flaherty