IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

FERRING PHARMACEUTICALS INC., FERRING INTERNATIONAL CENTER S.A., FERRING B.V., and POLYPEPTIDE LABORATORIES A/S Plaintiffs, v. FRESENIUS KABI USA, LLC, Defendant.	C.A. No. 20-431-MN

THIRD AMENDED COMPLAINT

Plaintiffs Ferring Pharmaceuticals Inc. ("Ferring Pharma"), Ferring International Center S.A. ("FICSA"), Ferring B.V. (collectively, "Ferring"), and Polypeptide Laboratories A/S ("PPL A/S") (together with Ferring, "Plaintiffs") bring this action against Defendant Fresenius Kabi USA, LLC ("Defendant") and allege as follows:

OVERVIEW

1. This is an action for infringement of United States Patent Number 9,579,359 ("the '359 patent"), United States Patent Number 9,415,085 ("the '085 patent"), United States Patent Number 8,841,081 ("the '081 patent"), United States Patent Number 9,877,999 ("the '999 patent"), United States Patent Number 8,828,938 ("the '938 patent"), United States Patent Number 10,695,398 ("the '398 patent"), United States Patent Number 10,729,739 ("the '739 patent"), and United States Patent Number 10,973,870 ("the '870 patent") (collectively, the

"patents in suit") under the Patent Laws of the United States, Title 35 of the United States Code, § 100 *et seq.* and for a declaratory judgment of infringement under 28 U.S.C. §§ 2201 and 2202.

2. This action arises out of Defendant's submission of Abbreviated New Drug Application ("ANDA") No. 211999 ("Defendant's ANDA") under Section 505(j) of the Federal Food, Drug, and Cosmetic Act ("the Act"), 21 U.S.C. § 355(j), seeking U.S. Food and Drug Administration ("FDA") approval to commercially manufacture, use, or sell a generic version of Ferring's FIRMAGON® (degarelix for injection) ("Defendant's ANDA Product") prior to the expiration of the '359 patent, the '085 patent, the '398 patent, the '739 patent, and the '870 patent.

THE PARTIES

3. Plaintiff Ferring Pharma is a private Delaware corporation having its principal place of business at 100 Interpace Parkway, Parsippany, New Jersey 07054.

4. Plaintiff FICSA is a Swiss private limited liability company having its offices at Ch. de la Vergognausaz 50, 1162 Saint-Prex, Switzerland.

5. Plaintiff Ferring B.V. is a Dutch private limited liability company having its offices at Polaris Avenue 144, Hoofddorp, 2132 JX, Netherlands.

6. Plaintiff PPL A/S is a company organized and existing under the laws of Denmark, having its registered offices at Herredsvejen 2 Hillerod, 3400 Denmark.

7. On information and belief, Defendant Fresenius USA is a corporation organized and existing under the laws of Delaware, with its principal place of business at Three Corporate Drive, Lake Zurich, Illinois 60047.

8. On information and belief, Fresenius Kabi AG is a corporation organized under the laws of Germany, with its principal place of business at Else-Kröner-Straße 1, 61352 Bad Homburg, Germany.

9. According to Defendant's Corporate Disclosure Statement Pursuant to Federal Rule of Civil Procedure 7.1 (D.I. 15), Defendant is wholly-owned by Fresenius Kabi Holding, LLC, which is wholly-owned by Fresenius Kabi AG.

10. Fresenius Kabi AG was originally named as a defendant in this litigation. (D.I. 1.)

11. On April 15, 2020, the parties filed a stipulation and order dismissing Fresenius Kabi AG without prejudice, subject to the agreements made in the stipulation. (D.I. 6.)

12. The Court ordered the stipulation and order on April 16, 2020. (D.I. 9.)

JURISDICTION AND VENUE

13. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

14. This Court has personal jurisdiction over Defendant because, on information and belief, it is organized under the laws of the State of Delaware and because Defendant is registered to conduct business within the State of Delaware (File No. 4373141). *See* https://icis.corp.delaware.gov/Ecorp/EntitySearch/NameSearch.aspx (accessed on March 10, 2020). On information and belief, Defendant maintains as a registered agent for service of process Corporation Service Company with an address at 251 Little Falls Drive, Wilmington, Delaware 19808.

15. This Court also has personal jurisdiction over Defendant because this suit arises out of and relates to its activities that are, and will be, directed to the State of Delaware. On information and belief, following any FDA approval of Defendant's ANDA, Defendant will market and sell Defendant's ANDA Product that is the subject of the infringement claims in this action in the State of Delaware and throughout the United States, including in this Judicial District.

16. On information and belief, Defendant, directly and through its subsidiaries, affiliates, or agents, is in the business of manufacturing generic pharmaceuticals that it distributes or has distributed in the State of Delaware and throughout the United States.

17. On information and belief, Defendant, acting in concert with Fresenius Kabi AG, prepared and filed Defendant's ANDA with the intention of seeking to market Defendant's ANDA Product nationwide, including within this Judicial District.

18. On information and belief, Defendant plans to market and sell Defendant's ANDA Product that is the subject of the infringement claims in this action in the State of Delaware, and throughout the United States, including within this Judicial District; list Defendant's ANDA Product on the State of Delaware's prescription drug formulary; and seek Medicaid reimbursement for sales of Defendant's ANDA Product in the State of Delaware, either directly or through one or more of Defendant's subsidiaries, agents, and/or alter egos.

19. On information and belief, Defendant knows and intends that, if approved, Defendant's ANDA Product will be distributed and sold in Delaware and will thereby displace sales of FIRMAGON®, causing injury to Plaintiffs. On information and belief, Defendant intends to take advantage of its established channels of distribution in Delaware for the sale of Defendant's ANDA Product.

20. This Court also has personal jurisdiction over Defendant by virtue of, *inter alia*, its activities that were purposefully directed to the State of Delaware. On information and belief, Defendant, in concert with Fresenius Kabi AG, filed Defendant's ANDA seeking approval to market Defendant's ANDA Product prior to the expiration of the '359 patent and '085 patent along with a Paragraph IV Certification regarding the '359 patent and '085 patent and sending its Notice Letter to Ferring Pharma, which is incorporated in Delaware. Thus, the consequences of

Defendant's actions were (and will be) suffered in Delaware, as Defendant knew or should have known.

21. This Court also has personal jurisdiction over Defendant because Defendant's contacts within this Judicial District are continuous and systematic. On information and belief, Defendant, in collaboration with Fresenius Kabi AG, develops, manufactures, seeks approval for, and sells FDA-approved generic pharmaceutical drugs that are regularly marketed, distributed, and sold in Delaware and throughout the United States. Thus, on information and belief, Defendant does substantial business in Delaware, derives substantial revenue from Delaware, and engages in other persistent courses of conduct in Delaware. These continuous and systematic contacts, including, but not limited to, those described above and below, are more than sufficient for this Court to exercise personal jurisdiction over Defendant.

22. Defendant regularly invokes the jurisdiction of the courts of this judicial district by filing patent infringement actions concerning FDA-approved drug products in this judicial district. *See, e.g.*, *Fresenius Kabi USA, LLC et al. v. Sagent Pharmaceuticals, Inc.*, C.A. No. 17-11-LPS, D.I. 1 (D. Del. Jan. 4, 2017); *Fresenius Kabi USA, LLC v. B. Braun Medical Inc.*, C.A. No. 16-250-RGA, D.I. 1 (D. Del. Apr. 11, 2016); *Fresenius Kabi USA, LLC v. Maia Pharmaceuticals, Inc.*, C.A. No. 16-237-GMS, D.I. 1 (D. Del. Apr. 7, 2016).

23. Defendant has not contested personal jurisdiction or venue in patent litigations concerning FDA-approved drug products in this judicial district. *See, e.g.*, *Millennium Pharmaceuticals, Inc. v. Fresenius Kabi USA, LLC et al*, C.A. No. 19-2252-CFC, D.I. 1, 8 (D. Del. Feb. 10, 2020); *Pharmacyclics LLC v. Fresenius Kabi USA, LLC*, C.A. No. 18-192-CFC, D.I. 80, 95 (D. Del. Feb. 11, 2019); *Spectrum Pharmaceuticals, Inc. et al v. Fresenius Kabi USA, LLC*, C.A. No. 18-1533-CFC, D.I. 1, 14 (D. Del. Nov. 8, 2018); *Merck Sharp & Dohme Corp. v.*

Fresenius Kabi USA, LLC, C.A. No. 18-196-MN, D.I. 1, 6 (D. Del. Mar. 16, 2018); *Onyx Therapeutics, Inc. v. Fresenius Kabi USA, LLC et al.*, C.A. No. 16-1012-LPS, D.I. 1, 19 (D. Del. Jan. 6, 2017); *Teva Pharmaceuticals International GmbH et al. v. Fresenius Kabi USA, LLC*, C.A. No. 17-1201-CFC, D.I. 1, 10 (D. Del. Sept. 15, 2017).

24. By stipulation ordered by the Court on April 16, 2020, Defendant agreed that it will not contest jurisdiction in this action and, as such would not move to dismiss this action for lack of personal jurisdiction. (D.I. 9 at ¶ 8.)

25. Venue is proper in this district pursuant to 28 U.S.C. § 1391(b) and (c) and § 1400(b) because Defendant is incorporated, and thus resides, in Delaware.

THE PATENTS IN SUIT

The ’359 Patent

26. On February 28, 2017, the United States Patent and Trademark Office (“PTO”) duly and legally issued the ’359 patent, which bears the title “Method of Treating Prostate Cancer with GnRH Antagonist” and names Tine Kold Olesen, Bo-Eric Persson, Per Cantor, Egbert A. van der Meulen, and Jens-Kristian Slott Jensen as inventors. A true and correct copy of the ’359 patent is attached as Exhibit A.

27. Ferring B.V. is the owner by assignment of the ’359 patent, and Ferring Pharma is an exclusive licensee of the ’359 patent.

28. The ’359 patent has one independent claim. Independent claim 1 of the ’359 patent states:

> **1**. A method of treating prostate cancer in a subject with a reduced likelihood of causing a testosterone spike or other gonadotrophin releasing hormone (GnRH) agonist side-effect comprising:
>
> administering an initial dose of 160-320 mg of degarelix to the subject, wherein the initial dose is administered as two subcutaneous injections; and
>
> administering a maintenance dose of 60-160 mg of degarelix to the subject once every 20-36 days thereafter, wherein the maintenance dose results in a testosterone suppression below 0.5 ng/mL;
>
> thereby treating prostate cancer in the subject with a reduced likelihood of causing a testosterone spike or other GnRH agonist side effect.

29. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '359 patent is listed in the FDA's APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (also known as the "Orange Book") as covering FIRMAGON®.

The '085 Patent

30. On August 16, 2016, the PTO duly and legally issued the '085 patent, which bears the title "Method of Treating Prostate Cancer with GnRH Antagonist" and names Egbert A. van der Meulen, and László Balázs Tankó as inventors. A true and correct copy of the '085 patent is attached as Exhibit B.

31. Ferring B.V. is the owner by assignment of the '085 patent, and Ferring Pharma is an exclusive licensee of the '085 patent.

32. The '085 patent has one independent claim. Independent claim 1 of the '085 patent states:

> 1. A method of treating prostate cancer in a subject, comprising:
>
> selecting a subject with a history of at least one cardiovascular event and prostate cancer;
>
> administering degarelix to the subject, wherein administration of degarelix to the subject decreases the frequency of an additional cardiovascular event in the subject as compared to the frequency of an additional cardiovascular event upon treatment with a gonadotrophin releasing hormone (GnRH) agonist in a subject with a history of at least one cardiovascular event,
>
> wherein the at least one cardiovascular event is chosen from myocardial infarction, ischemic heart disease, ischemic stroke, hemorrhagic stroke, and other arterial thrombotic/embolic events.

33. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '085 patent is listed in the Orange Book as covering FIRMAGON®.

The '081 Patent

34. On September 23, 2014, the PTO duly and legally issued the '081 patent, which bears the title "Method of Treating Metastatic Stage Prostate Cancer" and names Bo-Eric Persson as the inventor. A true and correct copy of the '081 patent is attached as Exhibit C.

35. FICSA is the owner by assignment of the '081 patent, and Ferring Pharma is an exclusive licensee of the '081 patent.

36. The '081 patent has two independent claims. For example, independent claim 15 of the '081 patent states:

> **15.** A method of treating metastatic stage prostate cancer in a subject. the method comprising:
>
> identifying a subject with metastatic stage prostate cancer comprising measuring the subject's baseline serum alkaline phosphatase (S-ALP) level and measuring the subject's baseline prostate-specific antigen (PSA) level; and
>
> reducing the subject's S-ALP level with respect to the baseline level by
>
> administering an initial dose of degarelix ranging from about 160 mg to about 320 mg to the subject; and
>
> administering at least one maintenance dose of degarelix ranging from about 60 mg to about 160 mg to the subject approximately 20 days to 36 days after the previous dose of degarelix for a duration of treatment.

The '999 Patent

37. On January 30, 2018, the PTO duly and legally issued the '999 patent, which bears the title "Method for Treating Metastatic Stage Prostate Cancer" and names Bo-Eric Persson as the inventor. A true and correct copy of the '999 patent is attached as Exhibit D.

38. FICSA is the owner by assignment of the '999 patent, and Ferring Pharma is an exclusive licensee of the '999 patent.

39. The '999 patent has five independent claims. For example, independent claim 15 of the '999 patent states:

> **15**. A method of treating a subject with metastatic prostate cancer having a serum alkaline phosphatase (S-ALP) level above a normal range for S-ALP prior to treatment, the method comprising:
>
> testing the prostate-specific antigen (S-ALP) and a prostate specific antigen (PSA) of a potential subject;
>
> selecting the potential subject for treatment if the subject's S-ALP is above the normal range for S-ALP and the PSA level is greater than or equal to 50 ng/mL;
>
> administering an initial dose of degarelix ranging from about 160 mg to about 320 mg to the subject; and
>
> administering at least one maintenance dose of degarelix ranging from about 60 mg to 160 mg to the subject, wherein the at least one maintenance dose is administered approximately 20 to 36 days after the previous dose of degarelix for a duration of treatment ranging from 20 days to 450 days; and further wherein the S-ALP level is reduced for the duration of treatment.

The '938 Patent

40. On September 9, 2014, the PTO duly and legally issued the '938 patent, which bears the title "Method for the Manufacture of Degarelix" and names Haixiang Zhang, Jens Fomsgaard, and Gunnar Staerkaer as inventors. A true and correct copy of the '938 patent is attached as Exhibit E.

41. PPL A/S is the owner by assignment of the '938 patent, and FICSA and its affiliates are an exclusive licensee of the '938 patent.

42. The '938 patent has one independent claim. Independent claim 1 of the '938 patent states:

> **1**. A method of manufacture of degarelix, Ac-D-2Nal-D-Phe(4Cl)-D-3Pal-Ser-4Aph(Hor)-D-4Aph(Cbm)-Leu-ILys-Pro-D-Ala-NH2, wherein Aph is 4-amino-phenylaniline, (Hor) is (L-hydroorotyl), and (Cbm) is (carbamoyl), containing 0.3% by weight or less of Ac-D-2Nal-D-Phe(4Cl)-D-3Pal-Ser-X-D-4Aph(Cbm)-Leu-ILys-Pro-D-Ala-NH2, wherein X is 4-([2-(5-hydantoyl)]acetylamino)-phenylalanine, comprising step-wise providing a solution of an amino acid or peptide in which an α-amino group is protected by Fmoc; contacting a solid support having an amino group linked thereto with the solution in the presence of reagent which forms a peptide bond between a carboxyl group of the dissolved amino acid or peptide and the amino group linked to the support for a time sufficient to form said peptide bond; removing Fmoc by contacting the support with an organic base selected from the group consisting of piperidine and C-alkyl substituted piperidine, wherein the alkyl is branched or straight chained and has from 1 to 6 atoms, in an organic solvent.

The '398 Patent

43. On June 30, 2020, the PTO duly and legally issued the '398 patent, which bears the title "Method of Treating Prostate Cancer with GnRH Antagonist" and names Egbert A. van der Meulen, and László Balázs Tankó as inventors. A true and correct copy of the '398 patent is attached as Exhibit P.

44. Ferring B.V. is the owner by assignment of the '398 patent, and Ferring Pharma is an exclusive licensee of the '398 patent.

45. The '398 patent has one independent claim. Independent claim 1 of the '398 patent states:

> **1**. A method for treating a subject that has prostate cancer with a gonadotrophin releasing hormone (GnRH) antagonist, the method comprising:
>
> selecting a subject that has a history of at least one cardiovascular event; and

administering degarelix to the subject having a history of at least one cardiovascular event,
wherein a risk of developing or experiencing an additional cardiovascular event upon treatment with degarelix is diminished compared to a risk of developing or experiencing an additional cardiovascular event upon treatment with a GnRH agonist, and
wherein the at least one cardiovascular event is chosen from myocardial infarction, ischemic heart disease, ischemic stroke, hemorrhagic stroke, and other arterial thrombotic/embolic events.

46. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '398 patent is listed in the Orange Book as covering FIRMAGON®.

The '739 Patent

47. On August 4, 2020, the PTO duly and legally issued the '739 patent, which bears the title "Method of Treating Prostate Cancer with GnRH Antagonist" and names Tine Kold Olesen, Bo-Eric Persson, Per Cantor, Egbert A. van der Meulen, and Jens-Kristian Slott Jensen as inventors. A true and correct copy of the '739 patent is attached as Exhibit Q.

48. Ferring B.V. is the owner by assignment of the '739 patent, and Ferring Pharma is an exclusive licensee of the '739 patent.

49. The '739 patent has three independent claims. For example, independent claim 1 of the '739 patent states:

> 1. A method of treating prostate cancer in a subject with a reduced likelihood of causing a testosterone spike or other gonadotrophin releasing hormone (GnRH) agonist side-effect comprising:
>
> administering an initial dose of 160-320 mg of degarelix to the subject, wherein the initial dose is administered subcutaneously; and
>
> administering a maintenance dose of 60-160 mg of degarelix to the subject once every 20-36 days thereafter for 364 days, wherein the maintenance dose results in a testosterone suppression below 0.5 ng/mL;
>
> wherein the testosterone suppression remains below 0.5 ng/mL to day 364 of treatment, and wherein the initial dose is administered as two subcutaneous injections.

50. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '739 patent is listed in the Orange Book as covering FIRMAGON®.

The '870 Patent

51. On April 13, 2021, the PTO duly and legally issued the '870 patent, which bears the title "Method of Treating Prostate Cancer with GnRH Antagonist" and names Tine Kold Olesen, Bo-Eric Persson, Per Cantor, Egbert A. van der Meulen, and Jens-Kristian Slott Jensen as inventors. A true and correct copy of the '870 patent is attached as Exhibit R.

52. Ferring B.V. is the owner by assignment of the '870 patent, and Ferring Pharma is an exclusive licensee of the '870 patent.

53. The '870 patent has two independent claims. For example, independent claim 1 of the '870 patent states:

> 1. A method of treating locally advanced prostate cancer in a subject, comprising:
>
> choosing a dosing regimen of degarelix over gonadotrophin releasing hormone (GnRH) agonist treatment to decrease the likelihood of developing a musculoskeletal disorder or a connective tissue disorder compared to GnRH agonist treatment when treating prostate cancer in the subject; and
>
> administering the dosing regimen of degarelix of an initial dose of 160-320 mg of degarelix to the subject and a maintenance

> dose of 60-160 mg of degarelix to the subject, wherein following the initial dose, the maintenance dose is administered once every 20-36 days thereafter.

54. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '870 patent is listed in the Orange Book as covering FIRMAGON®.

NATURE OF THE ACTION

55. Ferring Pharma is the holder of New Drug Application ("NDA") No. 022201 for FIRMAGON® (degarelix acetate) for injection, 80 mg and 120 mg.

56. On December 24, 2008, the United States Food and Drug Administration ("FDA") approved NDA No. 022201 for the manufacture, marketing, and sale of FIRMAGON® for treatment of patients with advanced prostate cancer.

57. Ferring Pharma has sold FIRMAGON® under NDA No. 022201 since its approval.

58. On information and belief, Defendant, in concert with Fresenius Kabi AG, filed Defendant's ANDA seeking approval to engage in the commercial manufacture, use, or sale in the United States of Defendant's ANDA Product before the expiration of the '359 patent and the '085 patent.

59. On information and belief, Defendant and Fresenius Kabi AG acted collaboratively and in concert in the preparation and submission of Defendant's ANDA and continue to act collaboratively in pursuing FDA approval of Defendant's ANDA and seeking to market Defendant's ANDA Product.

60. On information and belief, Defendant, in concert with Fresenius Kabi AG, made and included in Defendant's ANDA a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") that, in its opinion and to the best of its knowledge, the '359

patent and the ’085 patent are invalid, unenforceable, and/or will not be infringed by Defendant’s ANDA Product.

61. On February 11, 2020 and February 12, 2020, Ferring Pharma and Ferring B.V., respectively, received a letter from Defendant dated February 10, 2020, purporting to be a Notice of Certification for Defendant’s ANDA (“Defendant’s Notice Letter”) under Section 505(j)(2)(B)(ii) of the Act and 21 C.F.R. § 314.95(c)(1). Defendant’s Notice Letter enclosed a statement of alleged factual and legal bases that the ’359 patent and ’085 patent are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of Defendant’s ANDA Product (the “Detailed Statement”).

62. The Detailed Statement does not allege or provide any factual bases to assert non-infringement of claims 1-5, 7, 9-13 of the ’359 patent. The Detailed Statement also does not allege or provide any factual bases to assert that the ’359 patent or the ’085 patent is unenforceable.

63. On information and belief, Defendant, in concert with Fresenius Kabi AG, intends to seek permission from the FDA to market its ANDA Product prior to expiration of the ’398 patent, the ’739 patent, and the ’870 patent.

64. FDA regulations require that approved drug products include prescribing information reciting the FDA-approved indication(s) for the drug and related instructions for healthcare providers to safely and effectively administer the drug. *See* 21 C.F.R. § 201.56(a)(1)-(3), (d)(1); 21 C.F.R. § 201.57(a)-(c).

65. Consistent with FDA regulations, the package insert for FIRMAGON® includes prescribing information that recites the FDA-approved indication for FIRMAGON® and provides instructions for physicians and patients to safely and effectively administer FIRMAGON®.

66. Attached as Exhibit F is a true and correct copy of the February 2020 FIRMAGON® package insert, which is the current version of the FIRMAGON® package insert.

67. FIRMAGON® is indicated for the treatment of patients with advanced prostate cancer. (Ex. F at § 1.)

68. The recommended dosing information for FIRMAGON® is provided in Section 2.1 of the FIRMAGON® package insert as follows:

2.1 Dosing information

FIRMAGON is administered as a subcutaneous injection in the abdominal region only at the dosages in Table 1 below.

Table 1: FIRMAGON Recommended Dosages

Starting Dosage	Maintenance Dosage – Administered once every 28 days
• 240 mg given as two subcutaneous injections of 120 mg at a concentration of 40 mg/mL	• The first maintenance dose should be given 28 days after the starting dose. • 80 mg given as one subcutaneous injection at a concentration of 20 mg/mL

(Ex. F at § 2.1.)

69. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by a healthcare professional only:

2.2 Reconstitution and Administration Instructions

FIRMAGON is to be administered by a healthcare professional only.

(Ex. F at § 2.2.)

70. The "Dosage Form and Strengths" section of the FIRMAGON® package insert provides:

3 DOSAGE FORMS AND STRENGTHS

For injection:

- FIRMAGON (240 mg): Two single-dose vials each delivering 120 mg of degarelix in a white to off-white lyophilized powder for reconstitution supplied with diluent in two prefilled syringes.
- FIRMAGON (80 mg): One single-dose vial delivering 80 mg of degarelix in a white to off-white lyophilized powder for reconstitution supplied with diluent in one prefilled syringe.

(Ex. F at § 3.)

71. Section 5.3 of the FIRMAGON® package insert ("Laboratory Testing") states:

> **5.3 Laboratory Testing**
>
> FIRMAGON results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after FIRMAGON may be affected. The therapeutic effect of FIRMAGON should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

(Ex. F at § 5.3.)

72. Section 6.3 of the FIRMAGON® package insert ("Postmarketing Experience") states:

> **6.3 Postmarketing Experience**
>
> The following adverse reactions have been identified during post-approval use of FIRMAGON. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
>
> *Changes in bone density*
> Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with a GnRH agonist. It can be anticipated that long periods of medical castration in men will result in decreased bone density.

(Ex. F at § 6.3.)

73. Section 14 of the FIRMAGON® package insert ("Clinical Studies") states:

14 CLINICAL STUDIES

The safety and efficacy of FIRMAGON were evaluated in an open-label, multi-center, randomized, parallel-group study (NCT00295750) in patients with prostate cancer. A total of 620 patients were randomized to receive one of two FIRMAGON dosing regimens or leuprolide for one year:

a. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 80 mg (20 mg/mL) subcutaneously,
b. leuprolide 7.5 mg intramuscularly monthly.
c. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 160 mg (40 mg/mL) subcutaneously.

FIRMAGON is not approved for use with monthly doses of 160 mg (40 mg/mL) subcutaneously.

Serum levels of testosterone were measured at screening, on Day 0, 1, 3, 7, 14, and 28 in the first month, and then monthly until the end of the study.

The clinical trial population (n=610) across all treatment arms had an overall median age of approximately 73 (range 50 to 98). The ethnic/racial distribution was 84% white, 6% black and 10% others. Disease stage was distributed approximately as follows: 20% metastatic, 29% locally advanced (T3/T4 Nx M0 or N1 M0), 31% localized (T1 or T2 N0 M0) and 20% classified as other (including patients whose disease metastatic status could not be determined definitively - or patients with PSA relapse after primary curative therapy). In addition, the median testosterone baseline value across treatment arms was approximately 400 ng/dL.

The primary objective was to demonstrate that FIRMAGON is effective achieving and maintaining testosterone suppression to castration levels (T ≤ 50 ng/dL) during 12 months of treatment. The results are shown in Table 3.

Table 3: Medical Castration Rates (Testosterone ≤ 50 ng/dL) from Day 28 to Day 364

	FIRMAGON 240/80 mg N=207	**Leuprolide 7.5 mg N=201**
No. of Responders	202	194
Castration Rate (95% CIs)*	97.2% (93.5; 98.8)	96.4% (92.5; 98.2)

* Kaplan Meier estimates within group

Percentage changes in testosterone from baseline to Day 28 (median with interquartile ranges) are shown in Figure 2 and the percentages of patients who attained the medical castration of testosterone ≤ 50 ng/dL are summarized in Table 4.

Figure 2: Percentage Change in Testosterone from Baseline by Treatment Group until Day 28 (Median with Interquartile Ranges)

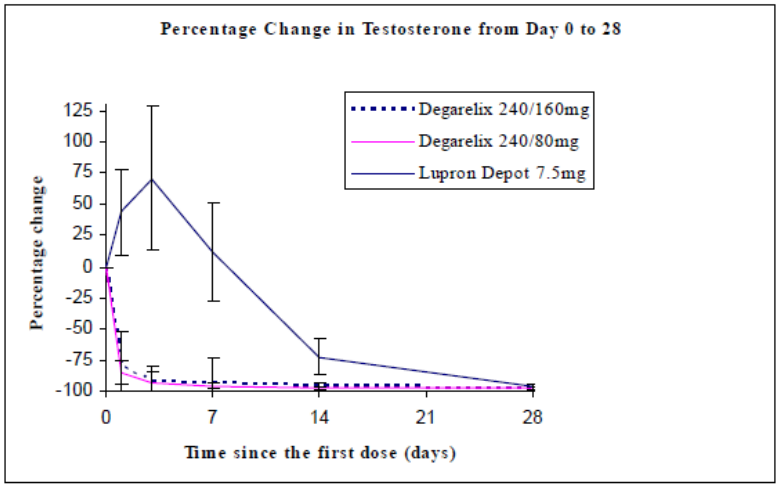

Table 4: Percentage of Patients Attaining Testosterone ≤ 50 ng/dL within the First 28 Days

	FIRMAGON 240/80 mg N=207	Leuprolide 7.5 mg N=201
Day 1	52%	0%
Day 3	96%	0%
Day 7	99%	1%
Day 14	99%	18%
Day 28	100%	100%

In the clinical trial, PSA levels were monitored as a secondary endpoint. PSA levels were lowered by 64% two weeks after administration of FIRMAGON, 85% after one month, 95% after three months, and remained suppressed throughout the one year of treatment. These PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline is related to a clinical benefit.

(Ex. F at § 14.)

74. The package insert for Defendant's ANDA Product will be substantially similar to the package insert for FIRMAGON® in all material respects.

75. Plaintiffs commenced this action within forty-five (45) days of receiving Defendant's Notice Letter.

76. There is an actual, real, immediate, and justiciable controversy between Plaintiffs and Defendant regarding whether Defendant will infringe the patents in suit.

COUNT I

Infringement of the '359 Patent

77. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

78. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '359 patent constitutes infringement of one of more claims of the '359 patent under 35 U.S.C. § 271(e)(2)(A).

79. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more claims of the '359 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

80. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

81. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '359 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

82. On information and belief, Defendant has knowledge of the '359 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '359 patent.

83. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

84. Plaintiffs have no adequate remedy at law.

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

COUNT II

Infringement of the '085 Patent

86. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

87. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '085 patent constitutes infringement of one of more claims of the '085 patent under 35 U.S.C. § 271(e)(2)(A).

88. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more claims of the '085 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

89. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

90. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '085 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

91. On information and belief, Defendant has knowledge of the '085 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '085 patent.

92. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

93. Plaintiffs have no adequate remedy at law.

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

COUNT III

Infringement of the '081 Patent

95. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

96. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '081 patent constitutes infringement of one of more claims of the '081 patent under 35 U.S.C. § 271(e)(2)(A).

97. 35 U.S.C. § 271(e)(2)(A) provides:

> It shall be an act of infringement to submit an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

98. The claims of the '081 patent are directed to "[a] method of treating metastatic stage prostate cancer."

99. "Metastatic stage prostate cancer" is a form of advanced prostate cancer.

100. FIRMAGON® is indicated for the treatment of patients with advanced prostate cancer. (Ex. F at § 1.)

101. These claims also arise under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

102. 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 this actual case or controversy requires a declaration of rights by this Court.

103. The '081 patent has two independent claims. For example, independent claim 15 of the '081 patent states:

> **15.** A method of treating metastatic stage prostate cancer in a subject. the method comprising:
> identifying a subject with metastatic stage prostate cancer comprising measuring the subject's baseline serum alkaline phosphatase (S-ALP) level and measuring the subject's baseline prostate-specific antigen (PSA) level; and
> reducing the subject's S-ALP level with respect to the baseline level by
> administering an initial dose of degarelix ranging from about 160 mg to about 320 mg to the subject; and
> administering at least one maintenance dose of degarelix ranging from about 60 mg to about 160 mg to the subject approximately 20 days to 36 days after the previous dose of degarelix for a duration of treatment.

104. The specification of the '081 patent states:

> One of the most important techniques for diagnosis of prostate cancer is blood testing; specifically, in the measurement of prostate-specific antigen (PSA) levels in the blood. The term [PSA] refers to a protein produced by cells of the prostate gland that is present in small quantities in the serum of normal men, but is often elevated in the presence of prostate cancer and in other prostate disorders. A blood test to measure PSA is the most effective test currently available for the

> early detection of prostate cancer. Levels of PSA, which are higher than normal, are associated with both localized and metastatic prostate cancer.

(Ex. C at 11:27-37.)

105. The specification of the ’081 patent further states that serum-alkaline phosphatase (“S-ALP”) testing “is well known in the art.” (Ex. C at 11:9 (citation omitted).) “Alkaline phosphatase (ALP) is a hydrolase enzyme responsible for removing phosphate groups from many types of molecules, including nucleotides, proteins, and alkaloids. In humans, ALP is present in all tissues throughout the entire body, but is particularly concentrated in liver, bile duct, kidney, bone and the placenta. (*Id.* at 10:58-63.) S-ALP testing is “generally used as a test of liver function, but is also known as an indicator for metastatic lesions in the bone for different malignancies (breast, prostate and colon). In metastatic prostate cancer, baseline S-ALP levels (or alternatively, ‘ALP levels’) are consistently higher than in localized or locally advanced disease reflecting bone lesions.” (*Id.* at 11:11-17.)

106. PSA testing is specifically recommended in Section 5.3 of the FIRMAGON® package insert. It states that “the therapeutic effect of FIRMAGON should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.” (Ex. F at § 5.3.)

107. The FIRMAGON® package insert warns of decreased bone density in men who have been treated with a GnRH antagonist. (Ex. F at § 6.3.)

108. Section 14 of the FIRMAGON® package insert discloses the results of a clinical trial, CS21, evaluating the safety and efficacy of FIRMAGON® in patients with prostate cancer (20% metastatic, 29% locally advanced, 31% localized, and 20% classified as other). (Ex. F at § 14.)

109. In CS21, "[a] total of 620 patients were randomized to receive one of two FIRMAGON dosing regimens or leuprolide for one year:

> a. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 80 mg (20 mg/mL) subcutaneously,
>
> b. leuprolide 7.5 mg intramuscularly monthly.
>
> c. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 160 mg (40 mg/mL) subcutaneously."

(Ex. F at § 14.)

110. As noted in the FIRMAGON® package insert, in CS21, PSA levels were monitored as a secondary endpoint. (Ex. F at § 14.) "PSA levels were lowered by 64% two weeks after administration of FIRMAGON, 85% after one month, 95% after three months, and remained suppressed throughout the one year of treatment." (*Id*.)

111. The package insert for Defendant's ANDA Product will be substantially similar to the package insert for FIRMAGON® in all material respects.

112. On information and belief, physicians or other healthcare providers reading the package insert for Defendant's ANDA Product and wanting to know more about the result of CS21 would look to peer-reviewed publications for a more detailed discussion of the study's findings.

113. Published peer-reviewed papers regarding CS21 indicate that "S-ALP and PSA levels were prospectively measured for all patients in CS21 as part of the laboratory tests included in the overall safety analysis and the secondary efficacy analyses, respectively" and report the results of CS21. (See, e.g., Schröder, FH et al. "Changes in Alkaline Phosphatase Levels in Patients with Prostate Cancer Receiving Degarelix or Leuprolide: Results from a 12-month, Comparative Phase III Study," 106 *BJU Int'l.* 182-187 (2009) ("Schröder 2009"; attached as Exhibit G) at 183; Schröder, FH et al. Abstract of "Degarelix Versus Leuprolide in

Patients with Prostate Cancer: Effect in Metastatic Patients as Assessed by Serum Alkaline Phosphatase," 8 *Euro. Urol. Supp.* 130 (2009); 130 at 40 ("Schröder 2009 Abstract"; attached as Exhibit H); Crawford, E. et al. "Prostate-specific Antigen and Serum Alkaline Phosphatase Levels in Prostate Cancer Patients Receiving Degarelix or Leuprolide," 183 *J. Urol* S866 (2010) ("Crawford 2010"; attached as Exhibit I); and Rick, F. et al. "An Update on the Use of Degarelix in the Treatment of Advanced Hormone-Dependent Prostate Cancer," 6 *Onco Targets and Therapy* 391-402 (2013) ("Rick 2013"; attached as Exhibit J).)

114. In Schröder 2009, the authors state that "[o]verall, 610 patients were included, with a median age of 73 years and median prostate-specific antigen (PSA) level of 19.0 ng/mL. Baseline S-ALP levels were high in metastatic patients and highest in patients with metastatic disease and a haemoglobin level of < 13 g/dL. In metastatic disease, after initial peaks in both groups, S-ALP levels were suppressed below baseline with degarelix but were maintained around baseline with leuprolide. The late rise in S-ALP seen with leuprolide was not apparent with degarelix." (Ex. G at Abstract.)

115. In Schröder 2009, the authors note that, "[a]ssessment of ALP levels before and during prostate cancer treatment might provide useful prognostic information. For example, ALP levels after 6 months of [androgen-deprivation therapy] were previously shown to be predictive of survival outcome in patients with prostate cancer." (Ex. G at 186.)

116. In Schröder 2009 Abstract, the authors state, "Patients with metastatic disease or those with PSA levels ≥ 50 ng/mL at baseline experience greater reductions in ALP with degarelix than leuprolide. Patients in the degarelix group maintained a suppression ALP throughout the study and did not display the signs of therapy failure, as seen for the leuprolide

patients. Results suggest better control of skeletal metastases with degarelix than leuprolide." (Ex. H at Conclusions.)

117. Later publications report that the results regarding S-ALP suppression seen in the pivotal clinical trial, CS21, were confirmed in a real world setting (*see* Geiges, G. et al. "Alkaline Phosphatase Control and Prostate Volume Reduction Under Degarelix Treatment in Prostate Cancer Patients Confirmed by Real Life Data from a German Registry," 187 *J. Urol.* e309: 757 (2012) ("Geiges 2012"; attached as Exhibit K); Geiges, G. et al. "Degarelix Therapy for Prostate Cancer in a Real-World Setting: Experience from the German IQUO (Association for Uro-Oncological Quality Assurance) Firmagon® Registry," 15 *BMC Urology* 122 (2015) ("Geiges 2015"; attached as Exhibit L)) and in a large, pooled patient population from five prospective phase 3 or 3b randomized trials (*see* Klotz, L. et al. "Disease Control Outcomes from Analysis of Pooled Individual Patient Data from Five Comparative Randomised Clinical Trials of Degarelix Versus Luteinising Hormone-Releasing Hormone Agonists," 66 *Euro. Urol.* 1101-1108 (2014) ("Koltz 2014"; attached as Exhibit M).)

118. Recent studies have further concluded that high S-ALP levels are associated with an increased risk of overall mortality and disease progression in patients with prostate cancer. (*See* Li, D. et al. "Prognostic Value of Serum Alkaline Phosphatase in the Survival of Prostate Cancer: Evidence from a Meta-Analysis," 10 *Cancer Mgmt. & Research* 3125-3139 (2018) ("Li 2018"; attached as Exhibit N); Mori, K. et al. "Prognostic Value of Alkaline Phosphatase in Hormone-sensitive Prostate Cancer: A Systemic Review and Meta-Analysis," 25 *Int'l. J. Clin. Oncol.* 247-257 (2020) ("Mori 2020"; attached as Exhibit O).) Thus, ALP is presently recognized as an "efficient and convenient biomarker for [prostate cancer] prognosis." (Ex. N at

3137) and is recommended to be "integrated into prognostic tools that help guide treatment strategy" (Ex. O at Abstract).

119. On information and belief, a physician or other healthcare provider following the FDA-approved package insert for Defendants' ANDA Product, and after a review of the literature, will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent.

120. On information and belief, a physician or other healthcare provider treating a patient with metastatic prostate cancer with Defendant's ANDA Product, and following the FDA-approved package insert for Defendants' ANDA Product and after a review of the literature, will measure the patient's PSA levels and S-ALP levels.

121. Defendant has made, and will continue to make, substantial preparation to manufacture, use, offer to sell, and/or sell within the United States, and/or to import into the United States, Defendant's ANDA Product prior to the expiration of the '081 patent.

122. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more of claims of the '081 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

123. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

124. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly

infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

125. On information and belief, Defendant has knowledge of the '081 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent.

126. European Patent No. 2 650 012 ("the EP '012 patent") is a European counterpart to the '081 patent. On December 22, 2015, Fresenius Kabi Deutschland GmbH filed a Notice of Opposition to the EP '012 patent requesting that the European Patent Office ("EPO") revoke the EP '012 patent in its entirety.

127. On information and belief, Fresenius Kabi Deutschland GmbH is wholly-owned by Fresenius Kabi AG. Thus, on information and belief, both Defendant and Fresenius Kabi Deutschland GmbH are wholly-owned by Fresenius Kabi AG.

128. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

129. Plaintiffs have no adequate remedy at law.

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

COUNT IV

Infringement of the '999 Patent

131. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

132. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United

States of Defendant's ANDA Product before the expiration of the '999 patent constitutes infringement of one of more claims of the '999 patent under 35 U.S.C. § 271(e)(2)(A).

133. 35 U.S.C. § 271(e)(2)(A) provides:

> It shall be an act of infringement to submit an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

134. The claims of the '999 patent are directed to, for example, "[a] method for treating a subject with metastatic stage prostate cancer."

135. "Metastatic stage prostate cancer" is a form of advanced prostate cancer.

136. FIRMAGON® is indicated for the treatment of patients with advanced prostate cancer. (Ex. F at § 1.)

137. These claims also arise under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

138. 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 this actual case or controversy requires a declaration of rights by this Court.

139. The '999 patent has five independent claims. For example, independent claim 15 of the '999 patent states:

> **15**. A method of treating a subject with metastatic prostate cancer having a serum alkaline phosphatase (S-ALP) level above a normal range for S-ALP prior to treatment, the method comprising:
>
> testing the prostate-specific antigen (S-ALP) and a prostate specific antigen (PSA) of a potential subject;
>
> selecting the potential subject for treatment if the subject's S-ALP is above the normal range for S-ALP and the PSA level is greater than or equal to 50 ng/mL;
>
> administering an initial dose of degarelix ranging from about 160 mg to about 320 mg to the subject; and
>
> administering at least one maintenance dose of degarelix ranging from about 60 mg to 160 mg to the subject, wherein the at least one maintenance dose is administered approximately 20 to 36 days after the previous dose of degarelix for a duration of treatment ranging from 20 days to 450 days; and further wherein the S-ALP level is reduced for the duration of treatment.

140. The specification of the '999 patent states:

> One of the most important techniques for diagnosis of prostate cancer is blood testing; specifically, in the measurement of prostate-specific antigen (PSA) levels in the blood. The term [PSA] refers to a protein produced by cells of the prostate gland that is present in small quantities in the serum of normal men, but is often elevated in the presence of prostate cancer and in other prostate disorders. A blood test to measure PSA is the most effective test currently available for the early detection of prostate cancer. Levels of PSA, which are higher than normal, are associated with both localized and metastatic prostate cancer.

(Ex. D at 11:46-57.)

141. The specification of the '081 patent further states that S-ALP testing "is well known in the art." (Ex. D at 11:28 (citation omitted).) "Alkaline phosphatase (ALP) is a hydrolase enzyme responsible for removing phosphate groups from many types of molecules, including nucleotides, proteins, and alkaloids. In humans, ALP is present in all tissues throughout the entire body, but is particularly concentrated in liver, bile duct, kidney, bone and the placenta." (*Id.* at 11:10-15.) S-ALP testing is "generally used as a test of liver function, but is also known as an indicator for metastatic lesions in the bone for different malignancies (breast,

prostate and colon). In metastatic prostate cancer, baseline S-ALP levels (or alternatively, 'ALP levels') are consistently higher than in localized or locally advanced disease reflecting bone lesions." (*Id.* at 11:31-36.)

142. PSA testing is specifically recommended in Section 5.3 of the FIRMAGON® package insert. It states that "the therapeutic effect of FIRMAGON should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured." (Ex. F at § 5.3.)

143. The FIRMAGON® package insert warns of decreased bone density in men who have been treated with a GnRH antagonist. (Ex. F at § 6.3.)

144. Section 14 of the FIRMAGON® package insert discloses the results of a clinical trial, CS21, evaluating the safety and efficacy of FIRMAGON® in patients with prostate cancer (20% metastatic, 29% locally advanced, 31% localized, and 20% classified as other). (Ex. F at § 14.)

145. In CS21, "[a] total of 620 patients were randomized to receive one of two FIRMAGON dosing regimens or leuprolide for one year:

> a. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 80 mg (20 mg/mL) subcutaneously,
>
> b. leuprolide 7.5 mg intramuscularly monthly.
>
> c. FIRMAGON at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 160 mg (40 mg/mL) subcutaneously."

(Ex. F at § 14.)

146. As noted in the FIRMAGON® package insert, in CS21, PSA levels were monitored as a secondary endpoint. (Ex. F at § 14.) "PSA levels were lowered by 64% two weeks after administration of FIRMAGON, 85% after one month, 95% after three months, and remained suppressed throughout the one year of treatment." (*Id.*)

147. The package insert for Defendant's ANDA Product will be substantially similar to the package insert for FIRMAGON® in all material respects.

148. On information and belief, physicians or other healthcare providers reading the package insert for Defendant's ANDA Product and wanting to know more about the result of CS21 would look to peer-reviewed publications for a more detailed discussion of the study's findings.

149. Published peer-reviewed papers regarding CS21 indicate that "S-ALP and PSA levels were prospectively measured for all patients in CS21 as part of the laboratory tests included in the overall safety analysis and the secondary efficacy analyses, respectively" and report the results of CS21. (See, e.g., Ex. G at 183; Ex. H; Ex. I; Ex. J.)

150. In Schröder 2009, the authors state that "[o]verall, 610 patients were included, with a median age of 73 years and median prostate-specific antigen (PSA) level of 19.0 ng/mL. Baseline S-ALP levels were high in metastatic patients and highest in patients with metastatic disease and a haemoglobin level of < 13 g/dL. In metastatic disease, after initial peaks in both groups, S-ALP levels were suppressed below baseline with degarelix but were maintained around baseline with leuprolide. The late rise in S-ALP seen with leuprolide was not apparent with degarelix." (Ex. G at Abstract.)

151. In Schröder 2009, the authors note that, "[a]ssessment of ALP levels before and during prostate cancer treatment might provide useful prognostic information. For example, ALP levels after 6 months of [androgen-deprivation therapy] were previously shown to be predictive of survival outcome in patients with prostate cancer." (Ex. G at 186.)

152. In Schröder 2009 Abstract, the authors state, "Patients with metastatic disease or those with PSA levels ≥ 50 ng/mL at baseline experience greater reductions in ALP with

degarelix than leuprolide. Patients in the degarelix group maintained a suppression ALP throughout the study and did not display the signs of therapy failure, as seen for the leuprolide patients. Results suggest better control of skeletal metastases with degarelix than leuprolide." (Ex. H at Conclusions.)

153. Later publications report that the results regarding S-ALP suppression seen in the pivotal clinical trial, CS21, were confirmed in a real world setting (*see* Exs. K, L) and in a large, pooled patient population from five prospective phase 3 or 3b randomized trials (*see* Ex. M.)

154. Recent studies have further concluded that high S-ALP levels are associated with an increased risk of overall mortality and disease progression in patients with prostate cancer. (*See* Ex. N; Ex. O.) Thus, ALP is presently recognized as an "efficient and convenient biomarker for [prostate cancer] prognosis." (Ex. N at 3137) and is recommended to be "integrated into prognostic tools that help guide treatment strategy" (Ex. O at Abstract).

155. On information and belief, a physician or other healthcare provider following the FDA-approved package insert for Defendants' ANDA Product, and after a review of the literature, will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent.

156. On information and belief, a physician or other healthcare provider treating a patient with metastatic prostate cancer with Defendant's ANDA Product, and following the FDA-approved package insert for Defendants' ANDA Product and after a review of the literature, will measure the patient's PSA levels and S-ALP levels.

157. Defendant has made, and will continue to make, substantial preparation to manufacture, use, offer to sell, and/or sell within the United States, and/or to import into the United States, Defendant's ANDA Product prior to the expiration of the '081 patent.

158. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more of claims of the '081 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

159. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

160. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

161. On information and belief, Defendant has knowledge of the '081 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent.

162. The EP '012 patent is a European counterpart to the '999 patent. On December 22, 2015, Fresenius Kabi Deutschland GmbH filed a Notice of Opposition to the EP '012 patent requesting that the EPO revoke the EP '012 patent in its entirety. On information and belief, Fresenius Kabi Deutschland GmbH is wholly-owned by Fresenius Kabi AG.

163. On information and belief, Fresenius Kabi Deutschland GmbH is wholly-owned by Fresenius Kabi AG. Thus, on information and belief, both Defendant and Fresenius Kabi Deutschland GmbH are wholly-owned by Fresenius Kabi AG.

164. Defendant has made, and will continue to make, substantial preparation to manufacture, use, offer to sell, and/or sell within the United States, and/or to import into the United States, Defendant's ANDA Product prior to the expiration of the '999 patent.

165. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more of claims of the '999 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

166. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

167. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '999 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

168. On information and belief, Defendant has knowledge of the '999 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '999 patent.

169. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

170. Plaintiffs have no adequate remedy at law.

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

COUNT V

Infringement of the '938 Patent

172. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

173. These claims arise under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

174. 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 this actual case or controversy requires a declaration of rights by this Court.

175. Prior to the invention of the '938 patent, significant risks were associated with methods to synthesize degarelix. For example, the '938 patent recognizes that the synthesis of degarelix is disclosed in U.S. Patent No. 5,925,730A ("the '730 patent"), but that the synthesis described therein included risks to both humans and the environment. (Ex. E at 3:10-23.) The synthesis described in the '730 patent uses trifluoroacetic acid ("TFA"), and it is known that "[a] disadvantage with TFA is its high human toxicity, which puts manufacturing personnel at risk." (*Id.*) Additionally, "[a]nother disadvantage with TFA is its environmental toxicity, which either makes it disposure costly or, if disposed improperly, contaminates the environment." (*Id.*)

176. The '938 patent states it as an object of the invention to provide a method for synthesizing degarelix that does not put human health at risk, as opposed to the method disclosed in the '730 patent. (Ex. E at 3: 27-30.) The '938 patent also states it is as an object of the invention to provide a method for synthesizing degarelix that does not put the environment at risk, as opposed to the method disclosed in the '730 patent. (*Id.* at 3:31-35.)

177. In addition to decreasing the risks to human health and/or the environment, in order for degarelix synthesis to be of use in the manufacture of pharmaceutical products, it also must be capable of producing degarelix in a sufficiently pure manner. To that end, the '938 patent notes:

> The inventors have surprisingly found that pharmaceutically pure degarelix can be manufactured by solid phase synthesis using Fmoc as α-amino protecting group. "Pharmaceutically pure" indicates the product does not contain more than 0.3% by weight of any single impurity. Unexpectedly the Aph(L-Hor) moiety does not undergo rearrangement during solid-phase synthesis in spite of being subjected to several cycles of Fmoc protection and deprotection under basic conditions.

(Ex. E at 3:46-54.)

178. Because of the risk to manufacturing personnel and the environment, on information and belief, no pharmaceutical company would use the methods described in the '730 patent to synthesize degarelix when another commercially viable means, as described in the '938 patent, is available. Moreover, any alternative method of manufacturing would have to be capable of producing sufficiently pure degarelix for use in pharmaceutical applications. Plaintiffs are not aware of any other commercially viable method of using solid-phase peptide synthesis to manufacture degarelix in sufficiently pure form that could be used to support Defendant's ANDA Product.

179. Similarly, on information and belief, no pharmaceutical company would use liquid-phase peptide synthesis in place of the process described in the '938 patent to manufacture degarelix for a new pharmaceutical product, such as Defendant's ANDA Product, because of issues with respect to efficiency and manufacturing costs.

180. European Patent No. 2421887 ("the EP '887 patent") is the European counterpart to the '938 patent.

181. The ’938 patent and the EP ’887 patent both claim priority to Swedish Patent Application No. SE 0900558 (“the SE ’558 application”).

182. Claim 1 of EP ’887 provides:

Claims

1. A method of manufacture of degarelix, Ac-D-2Nal-D-Phe(4Cl)-D-3Pal-Ser-4Aph(Hor)-D-4Aph(Cbm)-Leu-lLys-Pro-D-Ala-NH_2, wherein degarelix comprises 0.3 % by weight or less, in particular 0.1 % by weight or less, most particularly 0.01 % by weight or less, of Ac-D-2Nal-D-Phe(4Cl)-D-3Pal-Ser-X-D-4Aph(Cbm)-Leu-lLys-Pro-D-Ala-NH_2, wherein X is 4-([2-(5-hydantoyl)]acetylamino)-phenylalanine, the method comprising step-wise synthesis on a solid support comprising an amino group linked to the support, wherein the steps comprise providing a solution of an amino acid or peptide of which the α-amino group is protected by Fmoc; contacting the support with the solution in the presence of reagent for forming a peptide bond between a carboxyl group of the dissolved amino acid or peptide and the amino group linked to the support for a time sufficient to form said peptide bond; removing Fmoc by contacting the support with an organic base selected from piperidine and C-alkyl substituted piperidine, in particular 2-alkylpiperidine, 3-alkylpiperidine, 2,4-dialkylpiperidine, 2,5-dialkyl-piperidine, 2,6-dialkylpiperidine, wherein alkyl is branched or straight chain from 1 to 6 carbon, in particular methyl or ethyl, most particularly methyl, in an organic solvent.

183. Claim 1 of the EP ’887 patent is similar to claim 1 of the ’938 patent.

184. On January 22, 2016, Fresenius Kabi Deutschland GmbH filed a Notice of Opposition to the EP ’887 patent requesting that the EPO revoke the EP ’887 patent in its entirety.

185. On information and belief, Fresenius Kabi Deutschland GmbH is wholly-owned by Fresenius Kabi AG. Thus, on information and belief, both Defendant and Fresenius Kabi Deutschland GmbH are wholly-owned by Fresenius Kabi AG.

186. On information and belief, Fresenius Kabi Deutschland GmbH filed the Opposition to the EP ’887 patent in support of efforts related to the manufacture of degarelix for Defendant’s ANDA.

187. Because of the similarities between EP ’887 and the ’938 patent, on information and belief, the degarelix in Defendant’s ANDA will be synthesized according to the methods of the ’938 patent.

188. On information and belief, Fresenius entities often act in concert and across jurisdictions in attempting to invalidate patents that otherwise might be asserted against one or more Fresenius entities. Just because a specific Fresenius entity is not a named party in an action does not mean that it does not have an interest in that action.

189. Under U.S. law, a petitioner seeking to invalidate a patent according to inter partes review or post grant review must identify "all real parties in interest." 35 U.S.C. §§ 312, 322. Defendant has taken part in numerous patent challenges according to these provisions in which both Defendant and Fresenius Kabi Deutschland GmbH have been named as real parties in interest.

190. For example, in *Fresenius Kabi USA, LLC et al. v. Amgen, Inc.*, PTAB-IPR2019-01183, filed June 8, 2019, both Defendant (a named party) and Fresenius Kabi Deutschland GmbH (an unnamed party) are identified as real parties in interest. Similarly, in *Fresenius Kabi USA, LLC et al. v. Coherus Biosciences, Inc.*, PTAB-PGR2019-00064, filed September 17, 2019, both Defendant (a named party) and Fresenius Kabi Deutschland GmbH (again, an unnamed party) are identified as real parties in interest. In both these proceedings, numerous other Fresenius entities were also identified as real parties in interest.

191. On information and belief, the degarelix in Defendant's ANDA is synthesized according to the methods of the '938 patent, and Defendant and/or its affiliates have made, and will continue to make, substantial preparations to manufacture, use, offer to sell, and/or sell within the United States, and/or to import into the United States, Defendant's ANDA Product prior to the expiration of the '938 patent.

192. Even if Defendant does not make available information concerning the synthesis of the degarelix used in Defendant's ANDA Product, the lack of alternative commercially viable

methods to synthesize sufficiently pure degarelix for use in pharmaceutical applications related to new pharmaceutical products, such as Defendant's ANDA Product, would implicate the presumption of 35 U.S.C. § 295.

193. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA, Defendant's importation into the United States, and/or use, offer to sell, and/or sale within the United States, of Defendant's ANDA Product will constitute infringement, either literally or under the doctrine of equivalents, of one or more of claims of the '938 patent under 35 U.S.C. §§ 271(a) and/or (g).

194. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

195. Plaintiffs have no adequate remedy at law.

196. This case is an exceptional one, and Plaintiffs is entitled to an award of their reasonable attorneys' fees under 35 U.S.C. § 285.

COUNT VI

Infringement of the '398 Patent

197. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

198. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '398 patent constitutes infringement of one of more claims of the '398 patent under 35 U.S.C. § 271(e)(2)(A).

199. The '398 patent is listed in the Orange Book for NDA No. 022201.

200. Pursuant to 21 CFR §§ 314.107(b)(2) & 314.94(a)(12)(viii)(C)(1)(ii), Defendant must submit a certification for the '398 patent in connection with ANDA No. 211999 before obtaining FDA approval of the ANDA. On information and belief, Defendant has not submitted

a Paragraph III certification with ANDA No. 211999 for patents related to the '398 patent. Defendant has submitted a Paragraph IV certification in connection with ANDA No. 211999 for patents related to the '398 patent. On information and belief, Defendant intends to seek permission from the FDA to market its ANDA Product prior to the expiration of the '398 patent. Accordingly, a case or controversy exists between the parties regarding Defendant's infringement of the '398 patent.

201. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

202. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

203. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

204. On information and belief, Defendant has knowledge of the '398 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent.

205. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

206. Plaintiffs have no adequate remedy at law.

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

COUNT VII

Infringement of the '739 Patent

208. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

209. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '739 patent constitutes infringement of one of more claims of the '739 patent under 35 U.S.C. § 271(e)(2)(A).

210. The '739 patent is listed in the Orange Book for NDA No. 022201.

211. Pursuant to 21 CFR §§ 314.107(b)(2) & 314.94(a)(12)(viii)(C)(1)(ii), Defendant must submit a certification for the '739 patent in connection with ANDA No. 211999 before obtaining FDA approval of the ANDA. On information and belief, Defendant has not submitted a Paragraph III certification with ANDA No. 211999 for patents related to the '739 patent. Defendant has submitted a Paragraph IV certification in connection with ANDA No. 211999 for patents related to the '739 patent. On information and belief, Defendant intends to seek permission from the FDA to market its ANDA Product prior to the expiration of the '739 patent. Accordingly, a case or controversy exists between the parties regarding Defendant's infringement of the '739 patent.

212. Unless enjoined by this Court, upon FDA approval of Defendant's ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more claims of the '739 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

213. On information and belief, after the FDA has approved Defendant's ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant's ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant's ANDA Product.

214. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '739 patent by marketing Defendant's ANDA Product with the FDA-approved product insert.

215. On information and belief, Defendant has knowledge of the '739 patent and knows that the use of Defendant's ANDA Product in accordance with the FDA-approved product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '739 patent.

216. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

217. Plaintiffs have no adequate remedy at law.

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

COUNT VIII

Infringement of the '870 Patent

219. Plaintiffs reallege paragraphs 1 to 76 and incorporate them by reference.

220. Defendant's submission of ANDA No. 211999 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Defendant's ANDA Product before the expiration of the '870 patent constitutes infringement of one of more claims of the '870 patent under 35 U.S.C. § 271(e)(2)(A).

221. The ’870 patent is listed in the Orange Book for NDA No. 022201.

222. Pursuant to 21 CFR §§ 314.107(b)(2) & 314.94(a)(12)(viii)(C)(1)(ii), Defendant must submit a certification for the ’870 patent in connection with ANDA No. 211999 before obtaining FDA approval of the ANDA. On information and belief, Defendant has not submitted a Paragraph III certification with ANDA No. 211999 for patents related to the ’870 patent. Defendant has submitted a Paragraph IV certification in connection with ANDA No. 211999 for patents related to the ’870 patent. On information and belief, Defendant intends to seek permission from the FDA to market its ANDA Product prior to the expiration of the ’870 patent. Accordingly, a case or controversy exists between the parties regarding Defendant’s infringement of the ’870 patent.

223. Unless enjoined by this Court, upon FDA approval of Defendant’s ANDA No. 211999, Defendant will infringe, either literally or under the doctrine of equivalents, one or more claims of the ’870 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

224. On information and belief, after the FDA has approved Defendant’s ANDA No. 211999, Defendant intends to manufacture, market, sell, and offer to sell Defendant’s ANDA Product with an FDA-approved product insert that will direct physicians and patients in the use of Defendant’s ANDA Product.

225. On information and belief, Defendant will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Defendant knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the ’870 patent by marketing Defendant’s ANDA Product with the FDA-approved product insert.

226. On information and belief, Defendant has knowledge of the ’870 patent and knows that the use of Defendant’s ANDA Product in accordance with the FDA-approved

product insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '870 patent.

227. Plaintiffs will be irreparably harmed by Defendant's infringing activities unless those activities are enjoined by this Court.

228. Plaintiffs have no adequate remedy at law.

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

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully requests the following judgment and relief:

a. A declaration that the claims of United States Patent Number 9,579,359 are valid and enforceable;

b. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial manufacture, use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,579,359 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

c. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 9,579,359 will infringe one or more claims of United States Patent Number 9,579,359 under 35 U.S.C. § 271;

d. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 9,579,359, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

e. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 9,579,359 prior to the expiration date of United States Patent Number 9,579,359 and any additional dates of exclusivity;

f. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 9,579,359 and any additional dates of exclusivity;

g. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,579,359 and any additional dates of exclusivity;

h. A declaration that the claims of United States Patent Number 9,415,085 are valid and enforceable;

i. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,415,085 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

j. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of

United States Patent Number 9,415,085 will infringe one or more claims of United States Patent Number 9,415,085 under 35 U.S.C. § 271;

k. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 9,415,085, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

l. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 9,415,085 prior to the expiration date of United States Patent Number 9,415,085 and any additional dates of exclusivity;

m. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 9,415,085 and any additional dates of exclusivity;

n. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,415,085 and any additional dates of exclusivity;

o. A declaration that the claims of United States Patent Number 8,841,081 are valid and enforceable;

p. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 8,841,081 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

q. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 8,841,081 will infringe one or more claims of United States Patent Number 8,841,081 under 35 U.S.C. § 271;

r. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 8,841,081, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

s. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 8,841,081 prior to the expiration date of United States Patent Number 8,841,081 and any additional dates of exclusivity;

t. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 8,841,081 and any additional dates of exclusivity;

u. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant

engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 8,841,081 and any additional dates of exclusivity;

v. A declaration that the claims of United States Patent Number 9,877,999 are valid and enforceable;

w. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,877,999 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

x. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 9,877,999 will infringe one or more claims of United States Patent Number 9,877,999 under 35 U.S.C. § 271;

y. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 9,877,999, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

z. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 9,877,999 prior to the expiration date of United States Patent Number 9,877,999 and any additional dates of exclusivity;

aa. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 9,877,999 and any additional dates of exclusivity;

bb. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 9,877,999 and any additional dates of exclusivity;

cc. A declaration that the claims of United States Patent Number 8,828,938 are valid and enforceable;

dd. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 8,828,938 will infringe one or more claims of United States Patent Number 8,828,938 under 35 U.S.C. § 271;

ee. A permanent injunction under 35 U.S.C. § 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 8,828,938 prior to the expiration date of United States Patent Number 8,828,938 and any additional dates of exclusivity;

ff. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from

seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 8,828,938 and any additional dates of exclusivity;

gg. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 8,828,938 and any additional dates of exclusivity;

hh. A declaration that the claims of United States Patent Number 10,695,398 are valid and enforceable;

ii. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 10,695,398 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

jj. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 10,695,398 will infringe one or more claims of United States Patent Number 10,695,398 under 35 U.S.C. § 271;

kk. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 10,695,398, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

ll. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on

behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 10,695,398 prior to the expiration date of United States Patent Number 10,695,398 and any additional dates of exclusivity;

mm. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 10,695,398 and any additional dates of exclusivity;

nn. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 10,695,398 and any additional dates of exclusivity;

oo. A declaration that the claims of United States Patent Number 10,729,739 are valid and enforceable;

pp. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial manufacture, use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 10,729,739 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

qq. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 10,729,739 will infringe one or more claims of United States Patent Number 10,729,739 under 35 U.S.C. § 271;

rr. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 10,729,739, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

ss. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 10,729,739 prior to the expiration date of United States Patent Number 10,729,739 and any additional dates of exclusivity;

tt. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 10,729,739 and any additional dates of exclusivity;

uu. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product before the expiration of United States Patent Number 10,729,739 and any additional dates of exclusivity;

vv. A declaration that the claims of United States Patent Number 10,973,870 are valid and enforceable;

ww. A declaration that Defendant's submission to the FDA of Defendant's ANDA No. 211999 to obtain approval for the commercial manufacture, use, offer for sale, sale within, or importation into, the United States of Defendant's ANDA Product before the expiration of

United States Patent Number 10,973,870 was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

xx. A declaration that Defendant's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Defendant's ANDA Product prior to the expiration of United States Patent Number 10,729,739 will infringe one or more claims of United States Patent Number 10,973,870 under 35 U.S.C. § 271;

yy. An order that the effective date of the approval of Defendant's ANDA No. 211999 be a date that is not earlier than the expiration of the term of United States Patent Number 10,973,870, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

zz. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from infringing any claims of United States Patent Number 10,973,870 prior to the expiration date of United States Patent Number 10,973,870 and any additional dates of exclusivity;

aaa. A permanent injunction enjoining Defendant and all officers, agents, servants, employees, privies, and others acting for, or on behalf of, or in concert with any of them, from seeking, obtaining, or maintaining approval of ANDA No. 211999 until the expiration date of United States Patent Number 10,973,870 and any additional dates of exclusivity;

bbb. A judgment granting Plaintiffs compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Defendant engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United

States of Defendant's ANDA Product before the expiration of United States Patent Number 10,973,870 and any additional dates of exclusivity;

ccc. A judgment and order that this is an exceptional case under 35 U.S.C. § 285 and awarding Plaintiffs their reasonable attorneys' fees, costs, and expenses; and

ddd. Any and all other and further relief as this Court deems just and proper.

Dated: April 14, 2021

/s/ Mary W. Bourke
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