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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

FERRING PHARMACEUTICALS INC.; FERRING INTERNATIONAL CENTER S.A.; and FERRING B.V. Plaintiffs, v. JIANGSU HANSOH PHARMACEUTICAL GROUP CO., LTD., Defendant.	Civil Action No. 24-7904 *Document Filed Electronically*

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Ferring Pharmaceuticals Inc. ("Ferring Pharma"), Ferring International Center S.A. ("FICSA"), and Ferring B.V. (collectively, "Ferring") bring this action against Defendant Jiangsu Hansoh Pharmaceutical Group Co., Ltd. ("Hansoh") and allege as follows:

NATURE OF THE ACTION

1. This is an action for infringement of United States Patent Number 8,841,081 ("the '081 patent"), United States Patent Number 9,877,999 ("the '999 patent"), United States Patent Number 11,766,468 ("the '468 patent"), and United States Patent Number 11,826,397 ("the '397 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 Hansoh's submission of Abbreviated New Drug Application ("ANDA") No. 217496 ("Hansoh'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) ("Hansoh's ANDA Product") prior to the expiration of the '081, '999, '468, and '397 patents.

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. Upon information and belief, Defendant Hansoh is a corporation organized and existing under the laws of China, having a place of business at 9 Dongjin Road, Economic and Technical Development Zone, Lianyungang City, Jiangsu, 222069, China.

7. Upon information and belief, Hansoh prepared and filed ANDA No. 217496.

8. Upon information and belief, following any FDA approval of Hansoh's ANDA, Hansoh will manufacture, distribute, and/or sell Hansoh's ANDA Product throughout the United States, including in New Jersey.

JURISDICTION

9. This action arises under the patent laws of the United States, 35 U.S.C. §§ 100, et seq., and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, and this Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

10. Upon information and belief, this Court has personal jurisdiction over Hansoh because it has purposefully availed itself of the benefits and protections of New Jersey's laws such that it should reasonably anticipate being sued in this State. Upon information and belief, Hansoh, itself and through its agents, develops, manufactures, imports, offers to sell, markets, and/or sells generic drug products throughout the United States, including in New Jersey, and therefore transacts business within New Jersey related to Ferring's claims. This Court also has personal jurisdiction over Hansoh under Federal Rule of Civil Procedure 4(k)(2) because exercising jurisdiction over Hansoh is consistent with the United States Constitution and laws.

11. Upon information and belief, Hansoh (1) has substantial, continuous, and systematic contacts with New Jersey; (2) intends to market, sell, and/or distribute Hansoh's ANDA Product to the residents of New Jersey; (3) has corporate affiliates that are located in New Jersey; (4) maintains a distribution network within New Jersey; and/or (5) enjoys substantial income from sales of its generic pharmaceutical products in New Jersey.

12. Upon information and belief, Hansoh has purposefully availed itself of this forum by making, using, importing, selling, or offering to sell pharmaceutical products within New Jersey, including planning to distribute Hansoh's ANDA Product in New Jersey, and can therefore reasonably expect to be subject to jurisdiction in New Jersey's courts.

13. Upon information and belief, Hansoh has substantial, continuous, and systematic contacts with New Jersey including through its engagement in the direct marketing, distribution, and/or sales of generic pharmaceuticals within New Jersey.

14. Upon information and belief, Hansoh, and/or its subsidiaries, affiliates, or agents, intend to place Hansoh's ANDA Product into the stream of commerce with the reasonable expectation or knowledge, and the intent, that such product will be purchased and used by consumers in this District.

15. Upon information and belief, this Court has personal jurisdiction over Hansoh because, upon approval of ANDA No. 217496, Hansoh will distribute, market, offer for sale, sell, and/or import into the United States Hansoh's ANDA Product, including in New Jersey, and will derive substantial revenue from those actions in New Jersey.

VENUE

16. Ferring incorporates by reference the preceding paragraphs as if fully set forth herein.

17. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391 and 28 U.S.C. § 1400(b) because Hansoh is a foreign corporation that may be sued in any district in which it is subject to the court's personal jurisdiction, and upon information and belief, Hansoh is subject to this Court's personal jurisdiction.

THE PATENTS IN SUIT

The '081 Patent

18. On September 23, 2014, the United States Patent and Trademark Office ("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 A**.

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

The ’999 Patent

20. On January 30, 2018, the PTO duly and legally issued the ’999 patent, which bears the title “Methods 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 B**.

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

The ’468 Patent

22. On September 26, 2023, the PTO duly and legally issued the ’468 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 ’468 patent is attached as **Exhibit C**.

23. Ferring B.V. is the owner by assignment of the ’468 patent, and Ferring Pharma is an exclusive licensee of the ’468 patent.

24. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the ’468 patent is listed in the FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations (also known as the “Orange Book”) as covering FIRMAGON®.

The ’397 Patent

25. On November 28, 2023, the PTO duly and legally issued the ’397 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 ’397 patent is attached as **Exhibit D**.

26. Ferring B.V. is the owner by assignment of the ’397 patent, and Ferring Pharma is an exclusive licensee of the ’397 patent.

27. In accordance with 21 U.S.C. § 355(b)(1) and 21 C.F.R. § 314.53, the '397 patent is listed in the Orange Book as covering FIRMAGON®.

STATEMENT OF FACTS

Ferring's NDA and Hansoh's ANDA

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

29. 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.

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

31. Upon information and belief, Hansoh filed ANDA No. 217496 seeking approval to engage in the commercial manufacture, use, or sale in the United States of Hansoh's ANDA Product before the expiration of the '081, '999, '397, and '468 patents.

32. Upon information and belief, Hansoh prepared and submitted Hansoh's ANDA and continues to pursue FDA approval of Hansoh's ANDA and seeks to market Hansoh's ANDA Product.

33. Upon information and belief, Hansoh submitted a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") of invalidity, unenforceability, and/or noninfringement of the then-listed patents in the Orange Book as covering FIRMAGON®.

34. On September 27, 2022, Ferring Pharma received a letter from Hansoh purporting to be a Notice of Certification for Hansoh's ANDA ("Hansoh's Notice Letter") under Section 505(j)(2)(B)(i)-(iv) of the Act. Hansoh's Notice Letter enclosed a statement of alleged factual and legal bases that the then-listed patents in the Orange Book as covering FIRMAGON® allegedly

are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of Hansoh's ANDA Product (the "Detailed Statement").

35. The '397 and '468 patents both were issued by the PTO after the receipt of Hansoh's Detailed Statement and were subsequently listed in the Orange Book as covering FIRMAGON®.

36. Hansoh has not provided a Notice Letter directed to the '397 or '468 patent.

37. Upon information and belief, Hansoh intends to seek permission from the FDA to market its ANDA Product prior to expiration of the '081, '999, '397 and '468 patents.

38. There is an actual, real, immediate, and justiciable controversy between Ferring and Hansoh regarding whether Hansoh will infringe the patents in suit.

Prostate Cancer, Androgen Deprivation Therapy, and FIRMAGON

39. Prostate cancer is a leading cause of morbidity and mortality for men in the industrialized world. **Ex. C** at 1:13-14.

40. The majority of prostate cancers are dependent on testosterone for growth. **Ex. C** at 1:46-47. A current approach to treating advanced prostate cancer, which includes metastatic prostate cancer, involves administering treatments that interfere with the production of the hormone—luteinizing hormone ("LH")—that regulates the synthesis of androgen, which thereby contributes to the reduction of testosterone on which prostate cancers depend. **Ex. C** at 1:47-63. This method of treatment is referred to as androgen deprivation therapy ("ADT").

41. Modern forms of ADT include gonadotrophin releasing hormone ("GnRH") agonists and antagonists. **Ex. C** at 1:46-51, 3:22-25. GnRH agonists have been reported as a treatment for prostate cancer since at least 1985.

42. GnRH agonists treat prostate cancers by interacting with the GnRH receptors that stimulate the production of LH over a prolonged period of time, so that these receptors are

eventually desensitized, and LH is no longer produced. **Ex. C** at 1:64-2:13. However, the administration of GnRH agonists can cause an initial stimulation of LH production, which causes an increase in testosterone known as testosterone surge. **Ex. C** [468 patent] at 2:13-22. The testosterone surge caused by GnRH agonists can aggravate the patient's condition and cause other unwanted side effects. **Ex. C** at 2:22-28. GnRH agonists that have received FDA approval for the treatment of advanced prostate cancer include LUPRON DEPOT® (leuprolide), ELIGARD® (leuprolide acetate), TRELSTAR® (triptorelin pamoate for injectable suspension), VANTAS® (histrelin acetate), and ZOLADEX® (goserelin implant).

43. GnRH antagonists have been developed to overcome the testosterone surge associated with GnRH agonists. **Ex. C** at 2:37-40. GnRH antagonists block GnRH receptors and cause a rapid decrease of LH, thereby reducing testosterone production with no initial stimulation or surge. **Ex. B** at 2:35-39.

44. Ferring's pivotal Phase III study, CS21, evaluated the efficacy and safety of its GnRH antagonist, degarelix, compared to the GnRH agonist leuprolide. In CS21, 620 patients were randomized to one of three treatment groups, two of which administered degarelix at either a 240/160 mg dosing regimen or 240/80 mg dosing regimen, and one of which administered leuprolide at 7.5 mg. The degarelix-administered patients received an initiation dose as two subcutaneous injections on day 0 and a maintenance dose of one subcutaneous injection every 28 days. The leuprolide-administered patients received doses at day 0 and every 28 days via a single intramuscular injection. The results from CS21 demonstrated that degarelix, delivered at the 240/80 mg dosing regimen, produced a rapid and effective suppression in testosterone levels, which remained low throughout the 364-day treatment period. Further, degarelix suppressed testosterone significantly faster than leuprolide.

45. Ferring received FDA approval for FIRMAGON® (degarelix acetate) in 2008 for the treatment of advanced prostate cancer based on the results from CS21.

46. Ferring subsequently conducted a retrospective analysis of Ferring's CS21 study and CS21a extension study, focusing on serum alkaline phosphatase ("S-ALP"). Ferring discovered that there was an earlier suppression of S-ALP following degarelix treatment of metastatic prostate cancer patients than with leuprolide, and the magnitude and duration of the reduction was significantly greater with degarelix than with leuprolide. Moreover, towards the end of the one-year trial period, there was an increase in S-ALP with leuprolide, while no such increase was observed with degarelix. These findings underlie the invention claimed by the '081 and '999 patents.

47. Ferring also conducted a pooled analysis of its comparative clinical trials of degarelix versus GnRH agonists to ascertain whether there was a statistically significant difference in the cardiovascular effect from an agonist versus degarelix. The pooled analysis included data from 2,328 prostate cancer patients participating in two completed Phase 3 and four Phase 3b trials, all of which used an active comparator in the form of a GnRH agonist. The analysis showed that in patients with a history of cardiovascular events (specifically myocardial infarction, ischemic heart disease, ischemic stroke, hemorrhagic stroke, and other arterial thrombotic/embolic events), there was an approximately two-fold higher cardiovascular event rate in agonist versus degarelix treated patients. This pooled analysis forms the basis for the invention claimed in the '468 and '397 patents.

The FIRMAGON® Package Insert and Hansoh's Package Insert

48. FDA regulations require that approved drug products include prescribing information reciting the FDA-approved indication(s) for the drug and related instructions for

health care professionals ("HCPs") and patients 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).

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

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

51. Upon information and belief, the package insert for Hansoh's ANDA Product will be substantially similar to the package insert for FIRMAGON® in all material respects.

52. FIRMAGON® is indicated for the treatment of patients with advanced prostate cancer. **Ex. E** at § 1.

53. 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. E at § 2.1.

54. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by an HCP only:

2.2 Reconstitution and Administration Instructions

FIRMAGON is to be administered by a healthcare professional only.

Ex. E at § 2.2.

55. The "Warnings and Precautions" section of the FIRMAGON® package insert contains several warnings. **Ex. E** at § 5. None of these warnings provide that FIRMAGON® may increase the risk of cardiovascular disease.

56. The FIRMAGON® package insert package insert reports the results of Ferring's clinical study CS21 in Section 14 (Clinical Studies).

57. The FIRMAGON® package insert package insert states that in Ferring's CS21 clinical study, 20% of the subjects had metastatic prostate cancer, 29% of the subjects had locally advanced prostate cancer, 31% of the subjects had localized prostate cancer, and 20% of the subjects were classified as other. **Ex. E** at § 14.

COUNT I

Infringement of the '081 Patent

58. Ferring realleges paragraphs 1 to 57 and incorporates them by reference.

59. Hansoh's submission of ANDA No. 217496 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Hansoh's ANDA Product before the expiration of the '081 patent constitutes infringement of one of more claims of the '081 patent under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

60. There is an actual case or controversy such that the Court may entertain Ferring's 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.

61. Ferring asserts infringement of dependent claims 2, 7, 8, 9 and 10 of the '081 patent, all of which depend from independent claim 1 of the '081 patent.

62. Claims 1, 2, 7, 8, 9 and 10 of the '081 patent state:

> 1. 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
>
> reducing the subject's S-ALP level with respect to the baseline level by administering an initial dose of degarelix ranging from about 160 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, wherein the at least one maintenance dose is administered approximately 20 days 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 relative to the initial S-ALP level measured at the start of treatment.
>
> 2. The method of claim 1, wherein the initial dose of degarelix is about 240 mg, and the at least one maintenance dose of degarelix is about 80 mg administered to the subject approximately 28 days after the previous dose of degarelix.
>
> 7. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 60 IU/L from the baseline level between day 112 and day 364 of treatment.
>
> 8. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 50 IU/L from the baseline level between day 60 and day 364 of treatment.
>
> 9. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 50 IU/L from the baseline level between day 364 and day 450 of treatment.
>
> 10. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 90 IU/L from the baseline level between day 112 and day 364 of treatment.

63. An HCP administering Hansoh's ANDA Product in accordance with Hansoh's package insert will directly infringe claims 2, 7, 8, 9 and 10 of the '081 patent, either literally or under the doctrine of equivalents.

64. Upon information and belief, HCPs review and follow the package inserts for the drugs they use to treat their patients, and many are familiar with the relevant medical literature about the drugs they use to treat their patients.

65. Upon information and belief, an HCP administering Hansoh's ANDA Product will read and follow the package insert for Hansoh's ANDA Product.

66. Upon information and belief, Hansoh's package insert will be substantially similar to the package insert for FIRMAGON® in all material respects.

67. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by an HCP only. **Ex. E** at § 2.2.

68. Upon information and belief, an HCP will prescribe and administer Hansoh's ANDA Product pursuant to its FDA-approved indication for the treatment of patients with advanced prostate cancer. **Ex. E** at § 1.

69. Upon information and belief, at least some HCPs will use Hansoh's ANDA Product to treat patients with metastatic prostate cancer, which is a subset of advanced prostate cancer. Section 14 of the FIRMAGON® package insert demonstrates that 20% of patients in Ferring's CS21 study had metastatic prostate cancer. **Ex. E** at § 14.

70. S-ALP is a known biomarker for metastatic prostate cancer and, upon information and belief, at least some HCPs, in particular oncologists who treat urological cancers, measure S-ALP in their routine practice of diagnosing and treating patients with metastatic prostate cancer.

71. Upon information and belief, HCPs know that an elevated S-ALP level is an important predictor for bone metastasis. *See* **Ex. A** at 11:9-17.

72. Upon information and belief, at least some HCPs will identify a patient with metastatic prostate cancer for treatment with Hansoh's ANDA product by measuring the patient's baseline S-ALP level in addition to doing so using other diagnostic tools.

73. Upon information and belief, an HCP following Hansoh's package insert will administer an initial dose of 240 mg of Hansoh's ANDA Product to the patient. The recommended dosing information for FIRMAGON® provides that the initial dose is 240 mg. **Ex. E** at § 2.1.

74. Upon information and belief, an HCP following Hansoh's package insert will administer a maintenance dose of 80 mg of Hansoh's ANDA Product once every approximately 28 days to the patient for the duration of treatment. The recommended dosing information for FIRMAGON® provides that a maintenance dose of 80 mg should be given once every 28 days after the initial dose. **Ex. E** at § 2.1.

75. Upon information and belief, the S-ALP level of at least some metastatic prostate cancer patients who are administered Hansoh's ANDA Product in accordance with the dosing instructions in Hansoh's package insert will be reduced with respect to the patient's baseline S-ALP level for a duration of treatment ranging from 20 days to 450 days. This is supported by at least the mean and individual data of subjects administered FIRMAGON (to which Hansoh's ANDA Product, if approved, will have been deemed bioequivalent) in Ferring's CS21 and CS21a extension study. *See, e.g.*, **Ex. F** at 183-185 (reporting that S-ALP levels in patients with metastatic prostate cancer were reduced with respect to the baseline level by administering an initial 240 mg dose of degarelix followed by an 80 mg maintenance dose every 28 days for a year); **Ex. G** at Fig. 3 (results of Ferring's CS21A extension study demonstrating a reduction in S-ALP levels with respect to the baseline level in patients with metastatic stage prostate cancer over a duration of ranging from 20 days to 450 days that were administered degarelix 240/80 mg).

76. Upon information and belief, the S-ALP level of at least some metastatic prostate cancer patients who are administered Hansoh's ANDA Product in accordance with the dosing instructions in Hansoh's proposed package insert will be reduced (i) by at least 60 IU/L from the baseline level between day 112 and day 364 of treatment (claim 7), (ii) by at least 50 IU/L from the baseline level between day 60 and day 364 of treatment (claim 8), (iii) by at least 50 IU/L from the baseline level between day 364 and day 450 of treatment (claim 9), and (iv) by at least 90 IU/L from the baseline level between day 112 and day 364 of treatment. This is supported by at least the mean and individual data of subjects administered FIRMAGON (to which Hansoh's ANDA Product, if approved, will have been deemed bioequivalent) in Ferring's CS21 and CS21a extension study. *See, e.g.*, **Ex. F** at 183-185; **Ex. G** at Fig. 3.

77. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more of the asserted claims of the '081 patent by marketing, selling, and offering to sell Hansoh's ANDA Product with its package insert and in view of the knowledge and routine practice of HCPs, such as oncologists, who treat patients with metastatic prostate cancer.

78. Upon information and belief, Hansoh has knowledge of the '081 patent and knows that the use of Hansoh's ANDA Product in accordance with its package insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '081 patent.

79. Upon information and belief, Hansoh knows that at least some HCPs following Hansoh's package insert and as part of their routine practice will (i) identify patients with metastatic stage prostate cancer either by prior diagnoses, imaging techniques, and/or review of bloodwork that would include PSA, testosterone, and S-ALP, and (ii) administer degarelix to those

patients in accordance with the dosing instructions in Hansoh's package insert, which will reduce the S-ALP level for a duration of treatment in at least some of those patients.

80. Upon information and belief, Hansoh knows that HCPs have known for decades that high S-ALP levels are associated with an increased risk of overall mortality and disease progression in patients with prostate cancer.

81. Upon information and belief, Hansoh knows that S-ALP measurements are used alongside other techniques to diagnose and monitor bone metastases in prostate cancer patients.

82. Upon information and belief, Hansoh's package insert will encourage an HCP, such as an oncologist who specializes in urological cancers, to administer Hansoh's ANDA product to patients with metastatic prostate cancer. **Ex. E** at § 1 Indications and Usage (instructing that FIRMAGON is "indicated for treatment of patients with advanced prostate cancer"), § 14 Clinical Studies (instructing that 20% of the patients in the clinical study had metastatic prostate cancer).

83. Upon information and belief, S-ALP testing is part of routine bloodwork ordered by an oncologist both (i) when presented with a patient with potential metastatic prostate cancer and (ii) as part of routine monitoring of a metastatic prostate cancer patient during treatment with medical ADT.

84. Upon information and belief, an HCP, such as oncologist, would be encouraged by Hansoh's package insert to administer Hansoh's ANDA product to a patient with metastatic prostate cancer according to the claimed dosing regimen and would monitor that patient's S-ALP levels as part of routine testing.

85. Upon information and belief, through Hansoh's package insert (including the advanced prostate cancer indication and the clinical studies section describing that a portion of the patients in CS21 study had metastatic prostate cancer), Hansoh will encourage, direct, and lead at

least some HCPs to identify a patient with metastatic stage prostate cancer for treatment by measuring the patient's S-ALP levels, and to administer Hansoh's ANDA Product in accordance with the package insert, which will result in a reduction of the patient's S-ALP level with respect to the baseline level for a duration of treatment in at least some patients.

86. Upon information and belief, Hansoh has 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, Hansoh's ANDA Product prior to the expiration of the '081 patent.

87. Upon information and belief, after the FDA has approved Hansoh's ANDA No. 217496, Hansoh intends to manufacture, market, sell, and offer to sell Hansoh's ANDA Product with an FDA-approved product insert that will direct HCPs in the use of Hansoh's ANDA Product.

88. Unless enjoined by this Court, upon FDA approval of Hansoh's ANDA No. 217496, Hansoh will induce infringement by others of the asserted claims of the '081 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b).

89. Ferring will be irreparably harmed by Hansoh's infringing activities unless those activities are enjoined by this Court.

90. Ferring has no adequate remedy at law.

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

COUNT II

Infringement of the '999 Patent

92. Ferring realleges paragraphs 1 to 57 and incorporates them by reference.

93. Hansoh's submission of ANDA No. 217496 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United

States of Hansoh's ANDA Product before the expiration of the '999 patent constitutes infringement of one of more claims of the '999 patent under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

94. There is an actual case or controversy such that the Court may entertain Ferring's 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.

95. Ferring asserts infringement of dependent claims 2, 4, 5, 6, 7 and 8 of the '999 patent, all of which depend from independent claim 1 of the '999 patent.

96. Claims 1, 2, 4, 5, 6, 7 and 8 of the '999 patent state:

> 1. A method for treating a subject with metastatic stage prostate cancer having a serum alkaline phosphatase (S-ALP) level above a normal range for S-ALP prior to treatment, the method comprising:
>
> identifying a subject with metastatic stage prostate cancer having a S-ALP level above the normal range for S-ALP;
>
> reducing the subject's S-ALP 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 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.
>
> 2. The method of claim 1, wherein the initial dose of degarelix is about 240 mg, and the at least one maintenance dose of degarelix is about 80 mg administered to the subject approximately 28 days after the previous dose of degarelix.
>
> 4. The method of claim 1, wherein the subject to be treated is further identified by having a prostate-specific antigen (PSA) level greater than or equal to 50 ng/mL.
>
> 5. The method of claim 4, wherein the treated subject's S-ALP level is reduced by at least 60 IU/L between day 112 and day 364 of treatment.

> 6. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 50 IU/L between day 60 and day 364 of treatment.
>
> 7. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 50 IU/L between day 364 and day 450 of treatment.
>
> 8. The method of claim 1, wherein the treated subject's S-ALP level is reduced by at least 50 IU/L between day 364 and day 450 of treatment.

97. An HCP administering Hansoh's ANDA Product in accordance with Hansoh's package insert will directly infringe claims 2, 4, 5, 6, 7 and 8 of the '999 patent, either literally or under the doctrine of equivalents.

98. Upon information and belief, HCPs review and follow the package inserts for the drugs they use to treat their patients, and many are familiar with the relevant medical literature about the drugs they use to treat their patients.

99. Upon information and belief, an HCP administering Hansoh's ANDA Product will read and follow the package insert for Hansoh's ANDA Product.

100. Upon information and belief, Hansoh's package insert will be substantially similar to the package insert for FIRMAGON® in all material respects.

101. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by an HCP only. **Ex. E** at § 2.2.

102. Upon information and belief, an HCP will prescribe and administer Hansoh's ANDA Product pursuant to its FDA-approved indication for the treatment of patients with advanced prostate cancer. **Ex. E** at § 1.

103. Upon information and belief, at least some HCPs will use Hansoh's ANDA Product to treat patients with metastatic prostate cancer, which is a subset of advanced prostate cancer.

Section 14 of the FIRMAGON® package insert demonstrates that 20% of patients in Ferring's CS21 study had metastatic prostate cancer. **Ex. E** at § 14.

104. S-ALP is a known biomarker for metastatic prostate cancer, and, upon information and belief, at least some HCPs, in particular oncologists who treat urological cancers, measure S-ALP in their routine practice of diagnosing and treating patients with metastatic prostate cancer.

105. Upon information and belief, HCPs know that an elevated S-ALP level is an important predictor for bone metastasis. *See* **Ex. A** at 11:9-17, 27-37.

106. Upon information and belief, at least some HCPs will identify a patient with metastatic prostate cancer for treatment with Hansoh's ANDA product by measuring the patient's baseline S-ALP level in addition to doing so using other diagnostic tools.

107. Upon information and belief, an HCP following Hansoh's package insert will administer an initial dose of 240 mg of Hansoh's ANDA Product to the patient. The recommended dosing information for FIRMAGON® provides that the initial dose is 240 mg. **Ex. E** at § 2.1.

108. Upon information and belief, an HCP following Hansoh's package insert will administer a maintenance dose of 80 mg of Hansoh's ANDA Product once every approximately 28 days to the patient for the duration of treatment. The recommended dosing information for FIRMAGON® provides that a maintenance dose of 80 mg should be given once every 28 days after the initial dose. **Ex. E** at § 2.1.

109. Upon information and belief, the S-ALP level of at least some metastatic prostate cancer patients who are administered Hansoh's ANDA Product in accordance with the dosing instructions in Hansoh's package insert will be reduced with respect to the patient's baseline S-ALP level for a duration of treatment ranging from 20 days to 450 days. This is supported by at least the mean and individual data of subjects administered FIRMAGON (to which Hansoh's

ANDA Product, if approved, will have been deemed bioequivalent) in Ferring's CS21 and CS21a extension study. *See, e.g.*, **Ex. F** at 183-185 (reporting that S-ALP levels in patients with metastatic prostate cancer were reduced with respect to the baseline level by administering an initial 240 mg dose of degarelix followed by an 80 mg maintenance dose every 28 days for a year); **Ex. G** at Fig. 3 (results of Ferring's CS21A extension study demonstrating a reduction in S-ALP levels with respect to the baseline level in patients with metastatic stage prostate cancer over a duration of ranging from 20 days to 450 days that were administered degarelix 240/80 mg).

110. Upon information and belief, the S-ALP level of at least some metastatic prostate cancer patients who are administered Hansoh's ANDA Product in accordance with the dosing instructions in Hansoh's proposed package insert will be reduced (i) by at least 60 IU/L from the baseline level between day 112 and day 364 of treatment (claim 5), (ii) by at least 50 IU/L from the baseline level between day 60 and day 364 of treatment (claim 6), (iii) by at least 50 IU/L from the baseline level between day 364 and day 450 of treatment (claim 7), and (iv) by at least 90 IU/L from the baseline level between day 112 and day 364 of treatment. This is supported by at least the mean and individual data of subjects administered FIRMAGON (to which Hansoh's ANDA Product, if approved, will have been deemed bioequivalent) in Ferring's CS21 and CS21a extension study. *See, e.g.*, **Ex. F** at 183-185**; Ex. G** at Fig. 3.

111. Upon information and belief, at least some HCPs will further identify a patient with metastatic prostate cancer for treatment with Hansoh's ANDA product by measuring the patient's baseline PSA level and determining whether the patient has a PSA level greater than or equal to 50 ng/mL (claim 4).

112. Upon information and belief, HCPs who are presented with a patient with potential metastatic prostate cancer are going to do imaging as well as blood work to obtain baseline values

against which to monitor relevant levels over the duration of treatment, including the patient's PSA and S-ALP levels.

113. Upon information and belief, HCPs understand that a patient with a PSA level greater than 50 ng/mL most likely has bone metastases and therefore is likely to have an S-ALP level above the normal range. **Ex. F** at 182-187 (reporting the results of Ferring's ALP analysis and noted that, baseline levels of S-ALP "were highest in patients with metastatic disease and hemoglobin (Hb) levels of < 13g/dL" and that "baseline S-ALP levels were three to four times higher in patients with PSA levels of ≥ 50 ng/mL at baseline than in those with levels of <50 ng/mL.)

114. Upon information and belief, HCPs understand that while there is no exact correlation between PSA and ALP, the higher the PSA level, the more likely it is that the patient will have bone metastases and an elevated S-ALP level.

115. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more of the asserted claims of the '999 patent by marketing, selling, and offering to sell Hansoh's ANDA Product with its package insert and in view of the knowledge and routine practice of HCPs, such as oncologists, who treat patients with metastatic prostate cancer.

116. Upon information and belief, Hansoh has knowledge of the '999 patent and knows that the use of Hansoh's ANDA Product in accordance with its package insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '999 patent.

117. Upon information and belief, Hansoh knows that at least some HCPs following Hansoh's package insert and as part of their routine practice will (i) identify patients with

metastatic stage prostate cancer either by prior diagnoses, imaging techniques, and/or review of bloodwork that would include PSA, testosterone, and S-ALP, and (ii) administer degarelix to those patients in accordance with the dosing instructions in Hansoh's package insert, which will reduce the S-ALP level for a duration of treatment in at least some of those patients.

118. Upon information and belief, Hansoh knows that HCPs have known for decades that high S-ALP levels are associated with an increased risk of overall mortality and disease progression in patients with prostate cancer.

119. Upon information and belief, Hansoh knows that S-ALP measurements are used alongside other techniques to diagnose and monitor bone metastases in prostate cancer patients.

120. Upon information and belief, Hansoh's package insert will encourage an HCP, such as an oncologist who specializes in urological cancers, to administer Hansoh's ANDA product to patients with metastatic prostate cancer. **Ex. E** at § 1 Indications and Usage (instructing that FIRMAGON is "indicated for treatment of patients with advanced prostate cancer"), § 14 Clinical Studies (instructing that 20% of the patients in the clinical study had metastatic prostate cancer).

121. Upon information and belief, S-ALP testing is part of routine bloodwork ordered by an oncologist both (i) when presented with a patient with potential metastatic prostate cancer and (ii) as part of routine monitoring of a metastatic prostate cancer patient during treatment with medical ADT.

122. Upon information and belief, an HCP, such as oncologist, would be encouraged by Hansoh's package insert to administer Hansoh's ANDA product to a patient with metastatic prostate cancer according to the claimed dosing regimen and would monitor that patient's S-ALP levels as part of routine testing.

123. Upon information and belief, through Hansoh's package insert (including the advanced prostate cancer indication and the clinical studies section describing that a portion of the patients in CS21 study had metastatic prostate cancer), Hansoh will encourage, direct, and lead at least some HCPs to identify a patient with metastatic stage prostate cancer for treatment having a S-ALP level above 147 IU/L, and to administer degarelix in accordance with the package insert, which will result in reduction of the patient's S-ALP level in at least some patients.

124. Upon information and belief, Hansoh has 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, Hansoh's ANDA Product prior to the expiration of the '999 patent.

125. Upon information and belief, after the FDA has approved Hansoh's ANDA No. 217496, Hansoh intends to manufacture, market, sell, and offer to sell Hansoh's ANDA Product with an FDA-approved product insert that will direct HCPs in the use of Hansoh's ANDA Product.

126. Unless enjoined by this Court, upon FDA approval of Hansoh's ANDA No. 217496, Hansoh will induce infringement by others of the asserted claims of the '999 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b).

127. Ferring will be irreparably harmed by Hansoh's infringing activities unless those activities are enjoined by this Court.

128. Ferring has no adequate remedy at law.

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

COUNT III

Infringement of the '397 Patent

130. Ferring realleges paragraphs 1 to 57 and incorporates them by reference.

131. Hansoh's submission of ANDA No. 217496 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Hansoh's ANDA Product before the expiration of the '397 patent constitutes infringement of one of more claims of the '397 patent under 35 U.S.C. § 271(e)(2)(A).

132. Ferring asserts infringement of claims 1-8 and 10 of the '397 patent.

133. Independent claim 1 is a representative claim and states:

> 1. A method of treating a patient with prostate cancer comprising:
>
> selecting a patient with prostate cancer and a history of at least one cardiovascular event;
>
> administering to the patient with prostate cancer and a history of at least one cardiovascular event an initial dose of degarelix of 240 mg given as two subcutaneous injections of 120 mg each at a concentration of 40 mg/mL, and
>
> administering to the patient a maintenance dose of degarelix of 80 mg given as one subcutaneous injection at a concentration of 20 mg/mL, wherein the maintenance dose is administered approximately every 28 days after the previous dose of degarelix for a duration treatment,
>
> wherein the patient's risk of developing or experiencing an additional cardiovascular event is diminished compared to a risk of developing or experiencing an additional cardiovascular event upon treatment with a GnRH agonist,
>
> wherein the at least one cardiovascular event is one or more selected from myocardial infarction, ischemic heart disease, ischemic stroke, hemorrhagic stroke, and other arterial thrombotic/embolic events.

134. An HCP administering Hansoh's ANDA Product in accordance with Hansoh's package insert will directly infringe claims 1-8 and 10 of the '397 patent, either literally or under the doctrine of equivalents.

135. Upon information and belief, HCPs review and follow the package inserts for the drugs they use to treat their patients, and many are familiar with the relevant medical literature about the drugs they use to treat their patients.

136. Upon information and belief, an HCP administering Hansoh's ANDA Product will read and follow the package insert for Hansoh's ANDA Product.

137. Upon information and belief, Hansoh's package insert will be substantially similar to the package insert for FIRMAGON® in all material respects.

138. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by an HCP only. **Ex. E** at § 2.2.

139. Upon information and belief, an HCP will prescribe and administer Hansoh's ANDA Product pursuant to its FDA-approved indication for the treatment of patients with advanced prostate cancer. **Ex. E** at § 1.

140. Upon information and belief, at least some HCPs treating a patient with advanced prostate cancer will select a patient who has a history of at least one cardiovascular event, such as myocardial infarction, ischemic heart disease, ischemic stroke, or hemorrhagic stroke, for treatment with Hansoh's ANDA product.

141. Upon information and belief, at least some HCPs who treat prostate cancer are aware that many patients with prostate cancer have preexisting cardiovascular disease, which can lead to future cardiovascular events, and that cardiovascular disease is the leading cause of death in patients with prostate cancer.

142. Upon information and belief, at least some HCPs are aware that the administration of GnRH agonists carry an increased risk that patients will experience a cardiovascular event.

143. The American Heart Association, American Cancer Society, and American Urological Association published warnings in 2010 that there may be a relationship between ADT therapy with GnRH agonists and increased risk of cardiovascular disease. **Ex. H** at 838. Later that year, the FDA required all GnRH agonists to contain a cardiovascular safety warning in their package inserts. **Ex. I.** For instance, section 5.3 of the package insert for LUPRON DEPOT®, which is formulated with the GnRH agonist leuprolide, reads as follows:

> **5.3 Cardiovascular Diseases**
>
> Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice.

Ex. J at § 5.3 (Cardiovascular Diseases); *see also* **Ex. K** at § 5.4 (Cardiovascular Diseases); **Ex. L** at § 5.6 (Cardiovascular Diseases); **Ex. M** at § 5.5 (Cardiovascular Diseases); **Ex. N** at § 5.4 (Cardiovascular Diseases).

144. The package insert for FIRMAGON® does not include a cardiovascular safety warning. This absence instructs HCPs to choose degarelix over a GnRH agonist for prostate cancer patients that have a prior history of at least one cardiovascular event.

145. Upon information and belief, at least some HCPs who treat prostate cancer are aware that the package inserts for GnRH agonists contain a cardiovascular safety warning, and that the package insert for FIRMAGON® does not.

146. Upon information and belief, this difference in labeling demonstrates to at least some HCPs that treat prostate cancer that there is a greater risk of cardiovascular events when patients are treated with GnRH agonists compared to GnRH antagonists such as FIRMAGON®.

147. Upon information and belief, at least some HCPs who treat patients with prostate cancer are aware of the literature directed to cardiovascular risk and ADT, including the findings of Albertsen PC, et al., *Cardiovascular morbidity associated with gonadotrophin releasing hormone agonists and an antagonist*, 65 EUROPEAN UROL 565-73 (2014) ("Albertsen 2014"), attached as **Exhibit O**. Albertsen 2014 confirmed the findings of Example 2 of the '397 patent, namely that, among men with preexisting cardiovascular disease, the risk of cardiac events within one year of initiating therapy was significantly lower among men treated with degarelix compared with GnRH agonists.

148. Upon information and belief, an HCP following Hansoh's package insert will administer an initial dose of 240 mg of Hansoh's ANDA Product to the patient given as two subcutaneous injections of 120 mg each at a concentration of 40 mg/mL. The recommended dosing information for FIRMAGON® provides that the initial dose is 240 mg given as two subcutaneous injections of 120 mg each at a concentration of 40 mg/mL. **Ex. E** at § 2.1.

149. Upon information and belief, an HCP following Hansoh's package insert will administer a maintenance dose of 80 mg of Hansoh's ANDA Product given as one subcutaneous injection at a concentration of 20 mg/mL, wherein the maintenance dose is administered once every approximately 28 days to the patient for the duration of treatment. The recommended dosing information for FIRMAGON® provides that a maintenance dose of 80 mg given as one subcutaneous injection at a concentration of 20 mg/mL should be given once every 28 days after the initial dose. **Ex. E** at§ 2.1.

150. A healthcare provider who chooses to administer Hansoh's ANDA product in accordance with the dosing instructions in Hansoh's proposed package insert to a patient with advanced prostate cancer and a history of at least one CV event will diminish the patient's risk of

developing or experiencing an additional cardiovascular event compared to treatment with a GnRH agonist. **Ex. O** at 565 (Abstract). Other peer-reviewed literature has reported similar results among men with preexisting cardiovascular disease and advanced prostate cancer. **Ex. P** at 2187 (Abstract).

151. Upon information and belief, at least some patients who have a history of at least one cardiovascular event and who are selected by their HCP for treatment with Hansoh's ANDA product will have a history of myocardial infarction, ischemic heart disease, ischemic stroke, hemorrhagic stroke, or other arterial thrombotic/embolic events. *See, e.g.*, **Ex. O** at 569 (Tables 1, 3).

152. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more of the asserted claims of the '397 patent by marketing, selling, and offering to sell Hansoh's ANDA Product with its package insert and in view of the knowledge of HCPs who treat patients with advanced prostate cancer.

153. Upon information and belief, Hansoh has knowledge of the '397 patent and knows that the use of Hansoh's ANDA Product in accordance with its package insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '397 patent.

154. The '397 patent is listed in the Orange Book as covering FIRMAGON®, and Hansoh submitted a Paragraph IV certification to the FDA certifying that, in its opinion and to the best of its knowledge, each claim of the then-issued Orange Book patents allegedly is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the drug product described by Hansoh's ANDA. Upon information and belief, Hansoh similarly has or will certify that each claim of the '397 patent allegedly is invalid, unenforceable, and/or will not be

infringed by the commercial manufacture, use, or sale of the drug product described by Hansoh's ANDA.

155. Upon information and belief, Hansoh is aware of the cardiovascular advantages of administering degarelix to prostate cancer patients with a history of at least one CV event and knows that at least some HCPs will choose to administer Hansoh's ANDA product to those patients.

156. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '397 patent by marketing Hansoh's ANDA Product with the FDA-approved product insert along with the knowledge of a person of ordinary skill in the art.

157. Upon information and belief, through Hansoh's proposed package insert, Hansoh will encourage, direct, and lead at least some HCPs to select a patient with advanced prostate cancer and a history of at least one CV event for treatment with Hansoh's ANDA Product.

158. Upon information and belief, Hansoh has 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, Hansoh's ANDA Product prior to the expiration of the '397 patent.

159. Upon information and belief, after the FDA has approved Hansoh's ANDA No. 217496, Hansoh intends to manufacture, market, sell, and offer to sell Hansoh's ANDA Product with an FDA-approved product insert that will direct HCPs in the use of Hansoh's ANDA Product.

160. Unless enjoined by this Court, upon FDA approval of Hansoh's ANDA No. 217496, Hansoh will induce infringement by others of the asserted claims of the '397 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b).

161. Ferring will be irreparably harmed by Hansoh's infringing activities unless those activities are enjoined by this Court.

162. Ferring has no adequate remedy at law.

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

COUNT IV

Infringement of the '468 Patent

164. Ferring realleges paragraphs 1 to 57 and incorporates them by reference.

165. Hansoh's submission of ANDA No. 217496 to engage in the commercial manufacture, use, offer for sale, or sale within the United States or importation into the United States of Hansoh's ANDA Product before the expiration of the '468 patent constitutes infringement of one of more claims of the '468 patent under 35 U.S.C. § 271(e)(2)(A).

166. Ferring asserts infringement of claims 1-8 and 10 of the '468 patent.

167. Independent claim 1 is a representative claim and states:

> 1. A method of treating prostate cancer in a subject comprising:
>
> selecting a subject that has prostate cancer and a history of at least one cardiovascular event; and
>
> administering degarelix to the subject, wherein administering degarelix to the subject comprises administering to the patient an initial dose of degarelix of 240 mg given as two injections of 120 mg each, and administering to the patient a maintenance dose of degarelix of 80 mg given as one injection, wherein the maintenance dose is administered approximately every 28 days after the previous dose of degarelix for a duration treatment,

> wherein administering degarelix to the subject decreases the likelihood of developing or experiencing an additional cardiovascular event compared to treatment with a gonadotrophin releasing hormone (GnRH) agonist.

168. An HCP administering Hansoh's ANDA Product in accordance with Hansoh's package insert will directly infringe claims 1-8 and 10 of the '468 patent, either literally or under the doctrine of equivalents.

169. Upon information and belief, HCPs review and follow the package inserts for the drugs they use to treat their patients, and many are familiar with the relevant medical literature about the drugs they use to treat their patients.

170. Upon information and belief, an HCP administering Hansoh's ANDA Product will read and follow the package insert for Hansoh's ANDA Product.

171. Upon information and belief, Hansoh's package insert will be substantially similar to the package insert for FIRMAGON® in all material respects.

172. Section 2.2 of the FIRMAGON® package insert provides that FIRMAGON® is to be administered by an HCP only. **Ex. E** at § 2.2.

173. Upon information and belief, an HCP will prescribe and administer Hansoh's ANDA Product pursuant to its FDA-approved indication for the treatment of patients with advanced prostate cancer. **Ex. E** at § 1.

174. Upon information and belief, at least some HCPs treating a patient with advanced prostate cancer will select a patient who has a history of at least one cardiovascular event, such as myocardial infarction, ischemic heart disease, ischemic stroke, or hemorrhagic stroke, for treatment with Hansoh's ANDA product.

175. Upon information and belief, at least some HCPs who treat prostate cancer are aware that many patients with prostate cancer have preexisting cardiovascular disease, which can

lead to future cardiovascular events, and that cardiovascular disease is the leading cause of death in patients with prostate cancer.

176. Upon information and belief, at least some HCPs are aware that the administration of GnRH agonists carry an increased risk that patients will experience a cardiovascular event.

177. The American Heart Association, American Cancer Society, and American Urological Association published warnings in 2010 that there may be a relationship between ADT therapy with GnRH agonists and increased risk of cardiovascular disease. **Ex. H** at 838. Later that year, the FDA required all GnRH agonists to contain a cardiovascular safety warning in their package inserts. **Ex. I**. For instance, section 5.3 of the package insert for LUPRON DEPOT®, which is formulated with the GnRH agonist leuprolide, reads as follows:

> **5.3 Cardiovascular Diseases**
>
> Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice.

Ex. J at § 5.3 (Cardiovascular Diseases); *see also* **Ex. K** at § 5.4 (Cardiovascular Diseases); **Ex. L** at § 5.6 (Cardiovascular Diseases); **Ex. M** at § 5.5 (Cardiovascular Diseases); **Ex. N** at § 5.4 (Cardiovascular Diseases).

178. The package insert for FIRMAGON® does not include a cardiovascular safety warning. This absence instructs HCPs to choose degarelix over a GnRH agonist for prostate cancer patients that have a prior history of at least one cardiovascular event.

179. Upon information and belief, at least some HCPs who treat prostate cancer are aware that the package inserts for GnRH agonists contain a cardiovascular safety warning, and that the package insert for FIRMAGON® does not.

180. Upon information and belief, this difference in labeling demonstrates to at least some HCPs that treat prostate cancer that there is a greater risk of cardiovascular events when patients are treated with GnRH agonists compared to GnRH antagonists such as FIRMAGON®.

181. Upon information and belief, at least some HCPs who treat patients with advanced prostate cancer are aware of the literature directed to cardiovascular risk and ADT, including the findings of Albertsen PC, et al., *Cardiovascular morbidity associated with gonadotrophin releasing hormone agonists and an antagonist*, 65 EUROPEAN UROL 565-73 (2014) ("Albertsen 2014"). *See* **Ex. O**. Albertsen 2014 confirmed the findings of Example 2 of the '468 patent, namely that, among men with preexisting cardiovascular disease, the risk of cardiac events within one year of initiating therapy was significantly lower among men treated with degarelix compared with GnRH agonists.

182. Upon information and belief, an HCP following Hansoh's package insert will administer an initial dose of 240 mg of Hansoh's ANDA Product to the patient given as two injections of 120 mg each. The recommended dosing information for FIRMAGON® provides that the initial dose is 240 mg given as two subcutaneous injections of 120 mg each at a concentration of 40 mg/mL. **Ex. E** at § 2.1.

183. Upon information and belief, an HCP following Hansoh's package insert will administer a maintenance dose of 80 mg of Hansoh's ANDA Product given as one injection, wherein the maintenance dose is administered once every approximately 28 days to the patient for the duration of treatment. The recommended dosing information for FIRMAGON® provides that

a maintenance dose of 80 mg given as one subcutaneous injection at a concentration of 20 mg/mL should be given once every 28 days after the initial dose. **Ex. E** at § 2.1.

184. A healthcare provider who chooses to administer Hansoh's ANDA product in accordance with the dosing instructions in Hansoh's proposed package insert to a patient with advanced prostate cancer and a history of at least one CV event will decrease the likelihood of that patient developing or experiencing an additional cardiovascular event compared to treatment with a GnRH agonist. **Ex. O** at 565 (Abstract). Other peer-reviewed literature has reported similar results among men with preexisting cardiovascular disease and advanced prostate cancer. **Ex. P** at 2187 (Abstract).

185. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more of the asserted claims of the '468 patent by marketing, selling, and offering to sell Hansoh's ANDA Product with its package insert and in view of the knowledge of HCPs who treat patients with advanced prostate cancer.

186. Upon information and belief, Hansoh has knowledge of the '468 patent and knows that the use of Hansoh's ANDA Product in accordance with its package insert will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '468 patent.

187. The '468 patent is listed in the Orange Book as covering FIRMAGON®, and Hansoh submitted a Paragraph IV certification to the FDA certifying that, in its opinion and to the best of its knowledge, each claim of the then-issued Orange Book patents allegedly is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the drug product described by Hansoh's ANDA. Upon information and belief, Hansoh similarly has or will certify that each claim of the '468 patent allegedly is invalid, unenforceable, and/or will not be

infringed by the commercial manufacture, use, or sale of the drug product described by Hansoh's ANDA.

188. Upon information and belief, Hansoh is aware of the cardiovascular advantages of administering degarelix to prostate cancer patients with a history of at least one CV event and knows that at least some HCPs will choose to administer Hansoh's ANDA product to those patients.

189. Upon information and belief, Hansoh will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hansoh knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '468 patent by marketing Hansoh's ANDA Product with the FDA-approved product insert along with the knowledge of a person of ordinary skill in the art.

190. Upon information and belief, through Hansoh's proposed package insert, Hansoh will encourage, direct, and lead at least some HCPs to select a patient with prostate cancer and a history of at least one CV event for treatment with Hansoh's ANDA Product.

191. Upon information and belief, Hansoh has 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, Hansoh's ANDA Product prior to the expiration of the '468 patent.

192. Upon information and belief, after the FDA has approved Hansoh's ANDA No. 217496, Hansoh intends to manufacture, market, sell, and offer to sell Hansoh's ANDA Product with an FDA-approved product insert that will direct HCPs in the use of Hansoh's ANDA Product.

193. Unless enjoined by this Court, upon FDA approval of Hansoh's ANDA No. 217496, Hansoh will induce infringement by others of the asserted claims of the '468 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(b).

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

195. Ferring has no adequate remedy at law.

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

PRAYER FOR RELIEF

WHEREFORE, Ferring respectfully requests the following judgment and relief:

a. A declaration that the claims of the '081 patent are valid and enforceable;

b. A declaration that Hansoh's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product prior to the expiration of the '081 patent will infringe, directly or indirectly, one or more claims of the '081 patent under 35 U.S.C. § 271;

c. A permanent injunction under 35 U.S.C. § 283, enjoining Hansoh 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 the '081 patent prior to the expiration date of the '081 patent and any additional dates of exclusivity;

d. A permanent injunction enjoining Hansoh 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. 217496 until the expiration date of the '081 patent and any additional dates of exclusivity;

e. A judgment granting Ferring compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Hansoh engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product before the expiration of the '081 patent and any additional dates of exclusivity;

f. A declaration that the claims of the '999 patent are valid and enforceable;

g. A declaration that Hansoh's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product prior to the expiration of the '999 patent will, directly or indirectly, infringe one or more claims of the '999 patent under 35 U.S.C. § 271;

h. A permanent injunction under 35 U.S.C. § 283, enjoining Hansoh 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 the '999 patent prior to the expiration date of United States Patent Number 9,877,999 and any additional dates of exclusivity;

i. A permanent injunction enjoining Hansoh 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. 217496 until the expiration date of the '999 patent and any additional dates of exclusivity;

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

k. A declaration that the claims of the '397 patent are valid and enforceable;

l. A declaration that Hansoh's submission to the FDA of Hansoh's ANDA No. 217496 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Hansoh's ANDA Product before the expiration of the '397 patent was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

m. A declaration that Hansoh's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product prior to the expiration of the '397 patent will infringe, directly or indirectly, one or more claims of the '397 patent under 35 U.S.C. § 271;

n. An order under 35 U.S.C. § 271(e)(4)(A) that the effective date of the approval of Hansoh's ANDA No. 217496 be a date that is not earlier than the expiration of the term of the '397 patent, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Ferring is or becomes entitled;

o. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Hansoh 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 the '397 patent prior to the expiration date of the '397 patent and any additional dates of exclusivity;

p. A permanent injunction enjoining Hansoh 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. 217496 until the expiration date of the '397 patent and any additional dates of exclusivity;

q. A judgment granting Ferring compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Hansoh engages in the

manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product before the expiration of the '397 patent and any additional dates of exclusivity;

r. A declaration that the claims of the '468 patent are valid and enforceable;

s. A declaration that Hansoh's submission to the FDA of Hansoh's ANDA No. 217496 to obtain approval for the commercial use, offer for sale, sale within, or importation into, the United States of Hansoh's ANDA Product before the expiration of the '468 patent was an act of infringement under 35 U.S.C. § 271(e)(2)(A);

t. A declaration that Hansoh's manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product prior to the expiration of the '468 patent will infringe, directly or indirectly, one or more claims of United States Patent Number 11,766,468 under 35 U.S.C. § 271;

u. An order under 35 U.S.C. § 271(e)(4)(A) that the effective date of the approval of Hansoh's ANDA No. 217496 be a date that is not earlier than the expiration of the term of the '468 patent, including any extension(s) granted by the USPTO under 35 U.S.C. §§ 154 or 156, or any later expiration of exclusivity to which Ferring is or becomes entitled;

v. A permanent injunction under 35 U.S.C. §§ 271(e)(4)(B) and/or 283, enjoining Hansoh 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 the '468 patent prior to the expiration date of the '468 patent and any additional dates of exclusivity;

w. A permanent injunction enjoining Hansoh 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. 217496 until the expiration date of the '468 patent and any additional dates of exclusivity;

x. A judgment granting Ferring compensatory damages in an amount to be determined at trial and including both pre-judgment and post-judgment interest, if Hansoh engages in the manufacture, use, offer to sell, sale within, and/or importation into, the United States of Hansoh's ANDA Product before the expiration of the '468 patent and any additional dates of exclusivity;

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

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

Dated: July 19, 2024
Newark, New Jersey

Respectfully submitted,

s/ William P. Deni, Jr.
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