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

TOLMAR THERAPEUTICS, INC. and TOLMAR PHARMACEUTICALS, INC. Plaintiffs, v. FORESEE PHARMACEUTICALS CO., LTD. Defendants.	C.A. No. _____

COMPLAINT

Plaintiffs Tolmar Therapeutics, Inc. ("TTI") and Tolmar Pharmaceuticals, Inc. ("TPI") (collectively "Tolmar" or "Plaintiffs"), by its attorneys, for their Complaint, allege as follows:

1. This is an action for patent infringement under the patent laws of the United States, 35 U.S.C. § 100 et seq., and for a declaratory judgment of patent infringement under 28 U.S.C. §§ 2201 and 2202, that arises out of the submission of New Drug Application ("NDA") No. 211488 by Foresee Pharmaceuticals Co., Ltd. ("Foresee" or "Defendant") to the United States Food and Drug Administration ("FDA") seeking approval to commercially manufacture, use, sell, offer for sale, and/or import Defendant's proposed Camcevi® 42mg (leuprolide) injectable emulsion for the treatment of adult patients with advanced prostate cancer ("Camcevi product"), prior to the expiration of TTI's U.S. Patent No. 8,470,359.

THE PARTIES

2. Plaintiff TTI is a company organized under the laws of the State of Delaware with its principal place of business at 701 Centre Ave., Fort Collins, CO 80526.

3. TTI is the holder and owner of NDA Nos. 021379, 021488 and 021731 for Eligard® 22.5 mg, 30 mg, and 45 mg (leuprolide acetate) injectable. Tolmar's Eligard (leuprolide acetate) injectable products are approved by the FDA for the treatment of advanced prostate cancer.

4. TTI is the owner and assignee of U.S. Patent No. 8,470,359 (the "'359 patent"), which is listed in the FDA's publication Approved Drug Products With Therapeutic Equivalence Evaluations, also known as the "Orange Book" with respect to TTI NDA Nos. 021379, 021488 and 021731.

5. TPI is a company organized under the laws of the State of Delaware and has its principal place of business at 701 Centre Ave., Fort Collins, CO 80526. TPI is an exclusive licensee under the '359 patent.

6. On information and belief, Defendant Foresee is a company organized under the laws of Taiwan with its principal place of business at 9F-2., No.19-3, Sanchong Rd., Nangang Dist., Taipei City 115, Taiwan.

7. On information and belief, Defendant Foresee is in the business of, among other things, developing, manufacturing, selling, marketing, and distributing drugs, including distributing, selling and marketing drugs in the United States, including within the state of New Jersey, through its own actions and the actions of its agents, subsidiaries and/or licensees, from which Foresee derives or will derive a substantial portion of its revenue.

8. On information and belief, Defendant Foresee engaged the services of third-party NDA Regulatory Development, Inc. ("NDA Regulatory") as a consultant and US agent for the purposes of preparing and filing Foresee's NDA No. 211488. Exhibit A (May 25, 2021

correspondence from FDA to Foresee c/o NDA Regulatory attention Judith Plon granting final approval of NDA No. 211488).

9. On information and belief, NDA Regulatory is in the business of providing drug and medical device consultancy services, supporting companies in their drug/device development, regulatory submissions and clinical requirements and serves as a US agent for foreign companies leading the preparation and submission of their NDAs. *See* https://ndareg.com/. On further information and belief, NDA Regulatory has a principal place of business at 209 Princeton South Corporate Center, Suite 340, Ewing, NJ 0828. Exhibit A; https://ndareg.com/about-nda/.

JURISDICTION AND VENUE

10. This action arises under the patent laws of the United States of America and therefore this Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

11. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391 and 1400(b).

12. This Court has personal jurisdiction over Foresee because, upon information and belief, Foresee engaged third-party NDA Regulatory to prepare NDA No. 211488 and submit it to the FDA and to act as its US agent in the submission and subsequent FDA review of NDA No. 2111488. Exhibit A. On further information and belief, NDA No. 211488 was substantially prepared and filed with the FDA from NDA Regulatory's place of business at 200 Princeton South Corporate Center, Suite 340, Ewing, New Jersey 08628.

13. Further, this Court also has personal jurisdiction over Foresee because, among other things, on information and belief: (i) Foresee has filed NDA No. 211488 for the purpose of seeking approval to engage in the commercial manufacture, use, offer for sale, sell and/or

importation of the product described in NDA 211488 in the United States, including in the state of New Jersey; (ii) Foresee will, through its wholly owned subsidiary and/or its wholly owned affiliate and/or through its licensee, market, distribute, offer for sale, sell, use, and/or import into the United States the product described in NDA No. 211488 in the United States, including the state of New Jersey, and will derive substantial revenue from such activity in the state of New Jersey. *See Acorda Therapeutics v. Mylan Pharms. Inc.*, 817 F.3d 755, 763 (Fed. Cir. 2016). On information and belief, the product described in NDA No. 211488 would, among other things, be marketed, distributed, offered for sale, and/or sold in New Jersey, prescribed by physicians practicing in New Jersey, dispensed by pharmacies located in New Jersey and/or used by patients in New Jersey, all of which would have a substantial effect on New Jersey.

14. For at least the above reasons (and additional reasons to be further developed through discovery if necessary), this Court has personal jurisdiction over Foresee.

BACKGROUND

15. TPI, through a license from its affiliate TTI, commercially markets, offers for sale and sells ELIGARD® (leuprolide acetate) for injectable suspension in the United States. ELIGARD® (leuprolide acetate) for injectable suspension is indicated for the treatment of advanced prostate cancer and is marketed and sold in four dosages: 7.5 mg (one month); 22.5 mg (three months); 30 mg (four months); and 45 mg (six months). *See* https://eligard.com/about-eligard/

16. The '359 patent, entitled "Sustained Release Polymer" (Exhibit B hereto), was duly and legally issued on June 25, 2013. TTI is the owner and assignee of the '359 patent. TPI is an exclusive licensee under the '359 patent. The '359 patent is due to expire on October 15, 2023 and has been listed in connection with the 22.5 mg (three months), 30 mg (four months)

and 45 mg (six months) ELIGARD® (leuprolide acetate) for injectable suspension products in the Orange Book.

17. The '359 patent discloses and claims a "novel polymer composition for use in a sustained release formulation comprising the composition being emplaced within the tissue of a patient suffering from a malcondition such as prostate cancer." Exhibit B, col. 1, lines 15-21.

18. Claim 1 of the '359 patent recites:

> 1. A flowable composition for a controlled release formulation comprising
>
> an organic solvent,
>
> a medicament
>
> and a polymer of Formula
>
> HO—(P)—C(═O)O—R^a—O(O═)C—(P)—OH
>
> wherein:
>
> R^a is an alkane diradical comprising about 4 to about 8 carbons and is a residue of an alkane diol,
>
> P is a polymeric segment of repeating units of lactide, lactic, co(lactide-glycolide) or co(lactic-glycolic) moieties,
>
> the polymer is substantially insoluble in water and body fluid, the polymer has substantially no titratable carboxylic acid groups, and the polymer has a weight average molecular weight from about 10 kD to about 50 kD, and the polymer in neat form is a solid at ambient temperature,
>
> the organic solvent is a polar, aprotic organic solvent having at least some water solubility.

INFRINGEMENT BY FORESEE

19. Foresee submitted NDA No. 211488 to the FDA on July 27, 2020. Exhibit A. NDA No. 211488 was submitted "pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act ("FDCA") for CAMCEVI (leuprolide) injectable emulsion, for subcutaneous use."

Id. NDA No. 211488 is indicated for the treatment of adult patients with advanced prostate cancer. *Id.*

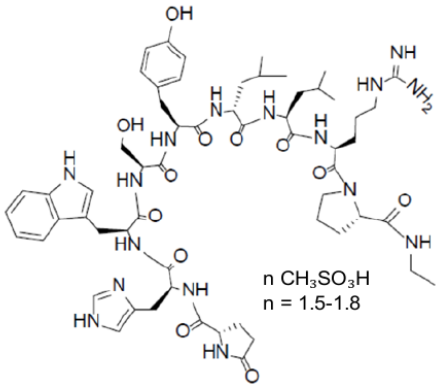
20. A copy of the label submitted to, and approved by, the FDA in connection with Foresee's NDA No. 211488 is attached hereto as Exhibit C.

21. The description of Foresee's Camcevi injectable product from the label approved by the FDA in connection with NDA No. 211488 is copied below:

11 DESCRIPTION

CAMCEVI is a sterile formulation of leuprolide mesylate for subcutaneous injection. CAMCEVI is designed to deliver approximately 42 mg of leuprolide over 6 months.

Leuprolide mesylate is a synthetic nonapeptide analog of naturally occurring GnRH and is a GnRH agonist. The analog possesses greater potency than the natural hormone. The chemical name is 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide mesylate (salt) with the following structural formula. The pH of 50 mg/mL solution of leuprolide mesylate in water is approximately 5.7.



CAMCEVI is supplied as a kit with a pre-filled, single-dose, sterile syringe for subcutaneous injection. Each pre-filled syringe delivers 42 mg leuprolide (equivalent to approximately 48 mg leuprolide mesylate), poly(D, L-lactide) (184 mg) polymer and *N*-methyl-2-pyrrolidone (136 mg).

22. The Camcevi injectable emulsion product described in NDA No. 211488 and the approved label ("Camcevi Product") is a flowable composition for a controlled release formulation and includes an organic solvent (N-methyl-2-pyrrolidone) and a medicament (leuprolide mesylate) as required by claim 1 of the '359 patent.

23. The Camcevi Product comprises leuprolide mesylate, which is a pharmaceutically acceptable salt of leuprolide. Exhibit C.

24. Each pre-filled syringe containing the Camcevi Product delivers 42 mg of leuprolide (equivalent to approximately 48 mg of leuprolide mesylate) over a period of six-months upon subcutaneous injection to a patient. Exhibit C.

25. The Camcevi Product also includes a poly(D, L-lactide) polymer. On information and belief, the poly(D, L-lactide) polymer is synthesized from D, L-lactide monomers with a laurel alcohol initiator ($C_{12}H_{25}OH$). Thus, the poly(D, L-lactide) polymer contains a hydroxyl (OH) end-group and an ester end-group.

26. The Camcevi Product meets the limitation of claim 1 of the '359 patent requiring a polymer having the formula HO—(P)—C(═O)O—R^a—O(O═)C—(P)—OH under the doctrine of equivalents. The poly(D, L-lactide) polymer used in the Camcevi Product is equivalent to the polymer in Claim 1 of the '359 patent having the formula HO—(P)—C(═O)O—R^a—O(O═)C—(P)—OH.

27. Upon information and belief, the poly(D,L-lactide) polymer used in the Camcevi Product has the formula R^a—O(O═)C—(P)—OH, where R^a has the formula $C_{12}H_{25}$. This polymer has insubstantial differences from the polymer in Claim 1 of the '359 patent which has the formula HO—(P)—C(═O)O—R^a—O(O═)C—(P)—OH.

28. The location of the R^a group—at the end of the polymer in the Camcevi Product compared to in the middle of the polymer in Claim 1—is an insubstantial difference in terms of the polymer formula. Given the number of polymeric repeating units, P, that make up both polymers, the R^a group in claim 1 and the equivalent R^a group in the Camcevi Product both make up less than 1% of the overall polymer weight. This is an insubstantial difference.

29. The location of the R^a group has an insignificant impact, if any, on the relevant properties of the polymer, including solubility, molecular weight, solid phase, and the absence of carboxylic acid groups. Specifically, the '359 patent notes that "[t]he chemical neutrality of the polymer is an outstanding advantage of the invention in that no acidic groups are present in the polymer to bring about auto-catalytic degradation." Exhibit B, col. 10, lines 3-8. The polymer in the Camcevi Product preserves the "outstanding advantage of the ['359 patent] invention in that no acidic groups are present." Thus, the polymer in the Camcevi Product has only insubstantial differences when compared to the polymer described in Claim 1.

30. The poly(D,L-lactide) polymer used in the Camcevi Product having the formula R^a —O(O═)C—(P)—OH, also provides the same function, in the same way, to achieve the same result as the polymer in Claim 1 of the '359 patent having the formula HO—(P)—C(═O)O—R^a—O(O═)C—(P)—OH.

31. Both the polymer in Claim 1 of the '359 patent and the poly(D, L-lactide) polymer used in the Camcevi Product provide the same function—a matrix for the controlled release of a medicament—in the same way—by forming a substantially solid depot upon contact with body fluid—to achieve the same result—the long term delivery of a medicament. Indeed, the polymer in Claim 1 and that used in the Camcevi Product both degrade ever time, allowing for the long-term delivery of a medicament.

32. The Camcevi Product meets the limitation of claim 1 of the '359 patent requiring a polymer having R^a, wherein "R^a is an alkane diradical comprising about 4 to about 8 carbons and is a residue of an alkane diol" under the doctrine of equivalents.

33. On information and belief, the poly(D, L-lactide) polymer used in the Camcevi Product is synthesized from D, L-lactide monomers using a lauryl alcohol initiator. During the

synthesis, an OH end-group from the lauryl alcohol initiator reacts with a carboxyl group of the D, L-lactide monomers. The result is a neutral polymer having a hydroxyl (-OH) end-group and an ester end-group. Accordingly, the R^a group in the polymer used in the Camcevi Product has the formula $C_{12}H_{25}$ and is a residue of the lauryl alcohol initiator. This R^a group is equivalent to the claimed R^a group in the '359 patent.

34. The R^a group in the polymer used in the Camcevi Product is insubstantially different that the R^a group described in claim 1 of the '359 patent. While the polymer used in the Camcevi Product has an R^a group containing 12 carbons, and the R^a group in claim 1 of the '359 patent requires about 4 to about 8 carbons, those differences are insubstantial. The R^a group makes up less than 1% of the overall polymer weight, so the addition of about 4 carbons is insubstantial to the function or structure of the R^a group in the claimed polymer formula. The R^a group in the Camcevi Product and the R^a group in claim 1 of the '359 patent are also similar chemically. Both R^a groups are alkyl alcohols, meaning they have fully saturated carbon atoms. As a result, both R^a groups react with the monomer to create a polymer without acidic groups.

35. The R^a group used in the Camcevi Product is derived from an alkane alcohol (i.e., lauryl alcohol having one hydroxyl group) instead of an alkane diol (having two hydroxyl groups) as described in claim 1 of the '359 patent. The use of an initiator having a single hydroxyl group results in the R^a group being located at the end of the polymer in the Camcevi Product compared to in the middle of the polymer in Claim 1. However, in the Camcevi Product, the end opposite the R^a group is identical to the end of the polymer described in claim 1. Moreover, as described above, the location of the R^a group has an insubstantial impact, if any, on the relevant properties of the polymer, including solubility, molecular weight, solid, phase, and the absence of acid groups. Specifically, the '359 patent notes that "[t]he chemical neutrality of

the polymer is an outstanding advantage of the invention in that no acidic groups are present in the polymer to bring about auto-catalytic degradation." Exhibit B, col. 10, lines 3-8. The use of an alkane alcohol (having one hydroxyl group) to initiate the polymer in the Camcevi Product preserves the "outstanding advantage of the ['359 patent] invention in that no acidic groups are present." Thus, the R^a group in the polymer of the Camcevi Product has only insubstantial differences when compared to the R^a group in the polymer described in Claim 1 of the '359 patent.

36. The R^a group in the polymer in the Camcevi Product also provides the same function, in the same way, to achieve the same result as the R^a group in the polymer described in Claim 1. Both R^a groups (i.e., the one in the Camcevi Product polymer and the one claimed in the '359 patent) are the residue of the initiator for the polymerization reaction to form the polymer. The initiator in both instances initiates ring-opening polymerization by reaction of the hydroxyl group of the initiator with a carbonyl group of the monomer to form polymeric segments (P). And in both instances, the end result is a polymer with substantially no terminal carboxylic acid groups. In the case of the Camcevi Product, the resulting polymer has an ester terminal group on one end and a hydroxyl terminal group on the other end, and substantially no terminal carboxylic acid groups.

37. The poly(D, L-lactide) polymer used in the Camcevi Product includes a polymeric segment of repeating units (P) of lactide as required by claim 1 of the '359 patent.

38. The poly(D, L-lactide) polymer used in the Camcevi Product is substantially insoluble in water and body fluid as required by claim 1 of the '359 patent.

39. Because the poly(D, L-lactide) polymer used in the Camcevi Product contains a hydroxyl (OH) end-group and an ester end-group, it has substantially no titratable carboxylic acid groups as required by claim 1 of the '359 patent.

40. On information and belief, the poly(D, L-lactide) polymer used in the Camcevi Product has an average molecular weight from about 10 kDa to about 50 kDa as required by claim 1 of the '359 patent.

41. The poly(D, L-lactide) polymer used in the Camcevi Product in neat form is a solid at ambient temperature as required by claim 1 of the '359 patent.

42. The organic solvent used in the Camcevi Product is N-methyl-2-pyrrolidone. Exhibit C. N-methyl-2-pyrrolidone is a polar, aprotic solvent having at least some water solubility as required by claim 1 of the '359 patent.

43. On information and belief, the FDA approved labeling for Foresee's Camcevi Product encourages, recommends, instructs and/or promotes administration of the Camcevi Product via a subcutaneous injection into the body tissue of a patient suffering from advanced prostate cancer. Exhibit C.

44. The purpose of Foresee's submission of NDA No. 211488 was to obtain approval under the FDCA to engage in the commercial manufacture, use, offer for sale, sale and/or importation of Foresee's Camcevi Product prior to the expiration of the '359 patent.

45. The FDA completed its review of NDA No. 211488 and granted final approval on May 25, 2021 for use of Foresee's Camcevi Product as recommended in the approved labeling. Exhibit A.

COUNT I
INFRINGEMENT OF U.S. PATENT NO. 8,470,359 UNDER 35 U.S.C. § 271(e)(2)

46. Tolmar incorporates each of the preceding paragraphs 1-45 as if fully set forth herein.

47. Foresee's submission of NDA No. 211488 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of Foresee's Camcevi Product prior to the expiration of the '359 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A). In the event that Foresee commercially manufactures, uses, offers for sale, sells and/or imports Foresee's Camcevi Product in the United States, said actions would constitute infringement of the '359 patent under 35 U.S.C. § 271(a).

48. The manufacture, use, offer for sale, sale, marketing, distribution and/or importation of Foresee's Camcevi Product (as described and approved in NDA No. 211488) would directly infringe at least claims 1, 11 and 12 of the '359 patent under the doctrine of equivalents.

49. On information and belief, Foresee will imminently engage in the manufacture, use, offer for sale, sale, marketing, distribution and/or importation into the United States of its Camcevi Product (as described and approved in NDA No. 211488).

50. The foregoing actions by Foresee constitute and/or will constitute infringement of the '359 patent.

51. On information and belief, Foresee has acted with full knowledge of the '359 patent and without a reasonable basis for believing that it was not and/or would not be liable for infringing the '359 patent.

52. Unless Foresee is enjoined from infringing the '359 patent, Tolmar will suffer irreparable injury for which there is no adequate remedy at law.

COUNT II
DECLARATORY JUDGMENT FOR INFRINGEMENT OF U.S. PATENT NO. 8,470,359

53. Tolmar incorporates each of the preceding paragraphs 1-52 as if fully set forth herein.

54. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution and/or importation of Foresee's Camcevi Product (as described and approved in NDA No. 211488) would directly infringe at least claims 1, 11 and 12 of the '359 patent under the doctrine of equivalents.

55. On information and belief, Foresee will imminently engage in the manufacture, use, offer for sale, sale, marketing, distribution and/or importation of its Camcevi Product (as described and approved in NDA No. 211488).

56. On information and belief, Foresee has acted with full knowledge of the '359 patent and without a reasonable basis for believing that it was not and/or would not be liable for infringing the '359 patent.

57. Accordingly, there is a real, substantial, and continuing case or controversy between Tolmar and Foresee regarding whether Foresee's manufacture, use, offer for sale, sale, marketing, distribution and/or importation into the United States of its Camcevi Product (as described and approved in NDA No. 211488) with its approved labeling will directly infringe at least claims 1, 11 and 12 of the '359 patent under the doctrine of equivalents.

58. Tolmar should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of Foresee's Camcevi Product with its approved labeling will directly infringe at least claims 1, 11 and 12 of the '359 patent under the doctrine of equivalents.

59. Foresee should be enjoined from infringing the '359 patent; otherwise Tolmar will suffer irreparable harm for which there is no adequate remedy at law.

REQUEST FOR RELIEF

WHEREFORE, Tolmar requests the following relief:

(a) a judgment that Foresee has infringed and/or will infringe the '359 patent under the doctrine of equivalents;

(b) a judgment that the asserted claims of the '359 patent are valid and enforceable;

(c) a preliminary and permanent injunction pursuant to, *inter alia*, 35 U.S.C. § 271(e)(4)(B) and 35 U.S.C. § 283 enjoining Foresee, its officers, agents, employees, and attorneys, and all persons working in concert with them from making, using, selling, offering for sale, marketing, distributing and/or importing into the United States Foresee's Camcevi Product or any product of which the making, using, offering for sale, sale, marketing, distribution, or importation infringes the '359 patent prior to the expiration date of the '359 patent, inclusive of any extension(s) and additional period(s) of exclusivity;

(d) a judgment declaring that making, using, selling, offering for sale, marketing, distributing, or importing Foresee's Camcevi Product, or any product the making, using, selling, offering for sale, marketing, distributing, or importation of which infringes the '359 patent, prior to the expiration date of the '359 patent;

(e) an award of Tolmar's damages or other monetary relief to compensate Tolmar if Foresee engages in the manufacture, use, offer for sale, sale, marketing, distribution or importation of Foresee's Camcevi Product, or any product the making, using, offering for sale, sale, marketing distribution, or importation of which infringes the '359 patent prior to the expiration date of the '359 patent, inclusive of any extension(s) and additional period(s) of exclusivity in accordance with 35 U.S.C. § 271(e)(4)(C);

(f) a declaration that this case against Foresee is an exceptional case and an award of attorneys' fees pursuant to 35 U.S.C. § 285;

(g) an award of Tolmar's costs and expenses in this action; and

(h) such further and other relief as this Court may deem just and proper.

Dated: August 20, 2021

/s/ Eric I. Abraham
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