UNITED STATES DISTRICT COURT
DISTRICT OF COLUMBIA

TAKEDA CHEMICAL INDUSTRIES, LTD., 475 Half Day Road, Suite 500 Lincolnshire, Illinois 60069, and TAKEDA PHARMACEUTICALS NORTH AMERICA, INC., 17-85 Jusohonmachi 2-chome Yogogawku, Osaka 532 Japan, Plaintiffs, *v.* ALPHAPHARM PTY, LTD., and GENPHARM, INC., Defendants.	Case No.

COMPLAINT

Plaintiffs, Takeda Chemical Industries, Ltd., ("TCI") and Takeda Pharmaceuticals North America, Inc., ("TPNA") (hereafter, collectively, "Takeda") by their undersigned counsel, for their Complaint against defendants Alphapharm Pty, Ltd., ("Alphapharm") and Genpharm, Inc., ("Genpharm") (collectively, "Defendants") allege as follows:

Jurisdiction and Venue

1. This is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code and arising under 35 U.S.C. §§ 271(e)(2),

271(b), and 281-283. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a). Venue is proper under 28 U.S.C. §§ 1391(b)-(d) and 1400(b).

Parties

2. TCI is a Japanese corporation having its corporate headquarters in Osaka, Japan and principal place of business in Osaka, Japan. TPNA is a wholly owned U.S. subsidiary of Takeda America Holdings, Inc., which is a wholly owned U.S. subsidiary of TCI. TPNA has its corporate headquarters and principal place of business in Lincolnshire, Illinois and is organized under the laws of Delaware.

3. TCI is engaged in the business of research, developing, manufacturing, and marketing of a broad spectrum of innovative pharmaceutical products, including ACTOS®, which comprises the active ingredient pioglitazone.

4. Upon information and belief, Alphapharm is an Australian company with its head office in Chase Building 2, Wentworth Park Road, Glebe NSW 2037 and manufacturing, research and development facilities in 15 Garnet Street, Carole Park QLD 4300, Australia. Upon information and belief, Abbreviated New Drug Application ("ANDA") No. 76-799 was filed under the name of Alphapharm. Upon information and belief, Alphapharm derives substantial revenue from interstate and/or international commerce, including commerce directed to the District of Columbia. By filing ANDA No. 76-799, Alphapharm has committed an act without the District of Columbia that

causes tortious consequences in the District of Columbia. Alphapharm has appointed an agent, pursuant to 21 C.F.R. § 314.95(c)(7), in the District of Columbia to accept service of process for commencement of this action.

5. Upon information and belief, defendant Genpharm is a Canadian company having a place of business in 85 Advance Rd, Etobicoke, Ontario, Canada M8Z-2S9. Upon information and belief, Genpharm imports drug products from Alphapharm into the U.S. Upon information and belief, Genpharm derives substantial revenue from interstate and/or international commerce, including commerce directed to the District of Columbia. Upon information and belief, by representing Alphapharm in connection with the filing of ANDA No. 76-799, Genpharm has committed an act without the District of Columbia that causes tortious consequences in the District of Columbia.

The New Drug Application

6. TPNA sells pioglitazone-containing drug products under the trade name ACTOS® in the United States pursuant to the United States Food and Drug Administration's approval of a New Drug Application ("NDA") held by TPNA (NDA NO. 021073).

7. ACTOS® is approved for use as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes (non-insulin-dependent diabetes

mellitus). ACTOS® may be used as the sole antidiabetic agent (monotherapy). ACTOS® may also be used in combination therapy with one or more different antidiabetic agents, such as an insulin secretion enhancer, e.g. sulfonylurea, a biguanide, e.g., metformin, and/or with insulin, when diet and exercise plus the single agent does not result in adequate glycemic control.

8. The approval letter for ACTOS®, with approved labeling, was issued by the FDA on July 15, 1999. The approval was for both monotherapy and combination therapy, based upon the FDA's consideration of clinical studies, presented in a single NDA, for both types of therapies.

The Patents in Suit

9. United States Patent No. 4,687,777 ("the '777 patent"), entitled "Thiazolidinedione Derivatives, Useful As Antidiabetic Agents," a true and correct copy of which is appended hereto as Exhibit A, was duly issued on August 18, 1987, to inventors Kanji Meguro and Takeshi Fujita, and assigned to plaintiff TCI. The '777 patent claims, *inter alia*, the novel compound commonly known under the nonproprietary name, "pioglitazone" [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-2,4- thiazolidinedione], and its pharmacologically acceptable salts. The '777 patent covers the drug approved in NDA No. 021073.

10. Plaintiff TCI has been and still is the owner through assignment of the '777 patent, which expires on January 17, 2011, having received a patent term extension under The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat 1585 (1984). 21 U.S.C. § 355 et seq.

11. United States Patent No. 5,965,584 ("the '584 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit B, was duly issued on October 12, 1999 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka and assigned to plaintiff TCI. The '584 patent claims, *inter alia*, a pharmaceutical composition comprising a pioglitazone or salts thereof in combination with a biguanide (e.g., metformin) and methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with treatment with a biguanide, such as metformin. Claim 13 recites that pioglitazone and biguanide are administered as an admixture. Claim 14 recites that pioglitazone and biguanide are administered independently.

12. Plaintiff TCI has been and still is the owner through assignment of the '584 patent, which expires on June 19, 2016.

13. United States Patent No. 6,329,404 ("the '404 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit C, was duly issued on December 11, 2001 to inventors Hitoshi Ikeda, Takashi

Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '404 patent claims, *inter alia*, a pharmaceutical composition comprising pioglitazone or salts thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea, such as glipizide, chlorpropamide, glyburide, tolazamide, and tolbutamide) and methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with treatment with an insulin secretion enhancer. Claim 24 recites that pioglitazone and an insulin secretion enhancer are administered as an admixture. Claim 25 recites that pioglitazone and an insulin secretion enhancer are administered independently.

14. Plaintiff TCI has been and still is the owner through assignment of the '404 patent, which expires on June 19, 2016.

15. United States Patent No. 6,150,383 ("the '383 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit D, was duly issued on November 21, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '383 patent claims, *inter alia*, methods for treating a glycometabolism disorder which comprise administering pioglitazone or salts thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

16. Plaintiff TCI has been and still is the owner through assignment of the '383 patent, which expires on June 19, 2016.

17. United States Patent No. 6,166,042 ("the '042 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit E, was duly issued on December 26, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '042 patent claims, *inter alia*, methods for treating a glycometabolism disorder which comprise administering pioglitazone or salts thereof in combination with a biguanide (e.g., metformin).

18. Plaintiff TCI has been and still is the owner through assignment of the '042 patent, which expires on June 19, 2016.

19. United States Patent No. 6,166,043 ("the '043 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit F, was duly issued on December 26, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '043 patent claims, *inter alia*, methods for reducing the amount of active components administered to a diabetic patient, which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with a biguanide (e.g., metformin).

20. Plaintiff TCI has been and still is the owner through assignment of the '043 patent, which expires on June 19, 2016.

21. United States Patent No. 6,172,090 ("the '090 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit G, was duly issued on January 9, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '090 patent claims, *inter alia*, methods for reducing the side effects of active components administered to a diabetic patient, which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with a biguanide (e.g., metformin), as the active components.

22. Plaintiff TCI has been and still is the owner through assignment of the '090 patent, which expires on June 19, 2016.

23. United States Patent No. 6,211,205 ("the '205 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit H, was duly issued on April 3, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '205 patent claims, *inter alia*, methods for reducing the amount of active components administered to a diabetic patient, which comprises administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

24. Plaintiff TCI has been and still is the owner through assignment of the '205 patent, which expires on June 19, 2016.

25. United States Patent No. 6,271,243 ("the '243 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit I, was duly issued on August 7, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '243 patent claims, *inter alia,* methods for reducing the side effects of active components administered to a diabetic patient, which comprises administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin preparation.

26. Plaintiff TCI has been and still is the owner through assignment of the '243 patent, which expires on June 19, 2016.

27. United States Patent No. 6,303,640 ("the '640 patent"), entitled "Pharmaceutical composition," a true and correct copy of which is appended hereto as Exhibit J, was duly issued on October 16, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TCI. The '640 patent claims, *inter alia,* methods for reducing the side effects of active components administering a therapeutically effective amount of a pioglitazone or salt thereof to a diabetic patient in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

. 28. Plaintiff TCI has been and still is the owner of all right, title and interest in the '640 patent, which expires on August 9, 2016.

29. Plaintiff TCI has granted an exclusive license to plaintiff TPNA under the '777 patent, the '584 patent, the '404 patent, the '383 patent, the '042 patent, the '043 patent, the '090 patent, the '205 patent, the '243 patent, and the '640 patent (collectively, "Takeda Patents").

30. In accordance with its exclusive license, plaintiff TPNA sells pioglitazone-containing drug products under the trade name ACTOS® in the United States. Sales of TPNA's pioglitazone-containing drug products are made pursuant to approval by the FDA of NDA NO. 021073.

31. Plaintiff TCI manufactures the pioglitazone-containing drug products sold by TPNA.

32. Plaintiffs TCI and TPNA will be both substantially and irreparably harmed by infringement of any of the Takeda Patents. There is no adequate remedy at law.

Count I

(Direct Infringement of U.S. Patent No. 4,687,777 Under 35 U.S.C. § 271(e)(2)(A) by Defendants)

33. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 32 above.

34. Upon information and belief, defendant Alphapharm filed an ANDA with the Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j) (ANDA No.76-799) seeking approval to market 15 mg, 30 mg, and 45 mg tablets comprising pioglitazone as its HCl salt.

35. By this ANDA filing, Defendants have indicated that they intend to engage, and that there is substantial likelihood that they will engage in the commercial manufacture, use, offer for sale, sale, and/or importation of plaintiffs' patented pioglitazone drug products immediately or imminently upon receiving FDA approval to do so. Also by Alphapharm's ANDA filing, Alphapharm has indicated that its drug products containing pioglitazone are bioequivalent to Takeda's pioglitazone drug products.

36. By this ANDA filing, Alphapharm seeks to obtain approval to commercially manufacture, use, offer for sale, sell, and/or import alleged generic equivalents of plaintiffs' ACTOS® pioglitazone drug products prior to the expiration date of the '777 patent.

37. By a letter ["The Letter"] dated January 29, 2004, Genpharm informed plaintiffs that Alphapharm had filed a certification to the FDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). A true and correct copy of The Letter is attached as Exhibit K. On or about February 4, 2004, NDA holder TPNA, received The Letter. On or about

February 9, 2004, patent owner, TCI, received a duplicate original of The Letter. The letter did not identify a U.S. agent for service of process for Alphapharm as required by 21 C.F.R. § 314.95(c)(7).

38. The Letter, purporting to be Alphapharm's Notice of Certification under 21 U.S.C.§ 355(j)(2)(B)(ii), alleges that in Alphapharm's opinion, its "the claims of the '777 patent are invalid, unenforceable, or will not be infringed."

39. Alphapharm asserts that claims 1 – 5 of the '777 patent are invalid under 35 U.S.C. § 102/103 in view of either of two references: U.S. Patent No. 4,287,200, and Sohda, et al., *Chem. Pharm. Bull. 30(10)*: 3580-3600 (1982). The United States Patent and Trademark Office considered both of those references during the prosecution of the '777 patent, and determined all of the claims of the '777 patent to be novel and unobvious in view of those references. Alphapharm further asserts that claim 3 is invalid under 35 U.S.C. § 112 for allegedly failing to provide an adequate written description in being drawn to a sodium salt of a compound that is not disclosed or described in the specification.

40. Defendants' filing of ANDA No. 76-799 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation or inducement thereof, of drug products containing pioglitazone or salts

thereof before the expiration of the '777 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

41. Defendants' manufacture, use, offer for sale, sale, and/or importation or inducement thereof, of the proposed pioglitazone drug product will directly infringe at least one of claims of the '777 patent.

42. Unless Defendants are enjoined from infringing and inducing the infringement of the '777 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

Count II

(Infringement of the '584 Patent Under 35 U.S.C. § 271(b))

43. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 42 above.

44. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale sale, and/or importation, or inducement thereof, of a drug product which is claimed and/or marketed and sold for use in a method claimed in one or more claims of the '584 patent, immediately or imminently upon approval of the ANDA.

45. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of

the '584 patent in combination therapy. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides, for use in methods covered by one or more claims of the '584 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of Defendants (e.g., including, without limitation, a physician, pharmacist, pharmacy benefits management company, health care provider who establishes drug formularies for its insurers, and/or patient).

46. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and their customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '584 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

47. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides, and such information will promote the use of pioglitazone in combination with a biguanide such as metformin. The beneficial effects of such co-administration and/or interactions are well known to Defendants' customers. By including this information in the label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '584 patent. Defendants know or reasonably should know that their proposed conduct will induce infringement.

48. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website which is accessible in the U.S. and promoting these its generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and indicate to consumers that it is an alternative to ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®,

which includes directions relating to the use of combinations of ACTOS® and a biguanide, also applies to Defendants' generic pioglitazone-containing drug product.

49. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

50. Plaintiffs will be substantially and irreparably harmed if defendants are not enjoined from inducing the infringement of the '584 patent. Plaintiffs have no adequate remedy at law.

Count III

(Infringement of the '404 Patent Under 35 U.S.C. § 271(b))

51. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 50 above.

52. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, sale, and/or importation or inducement thereof, of a drug product which is claimed and/or marketed and sold for use in a methods claimed in one or more claims of the '404 patent, immediately or imminently upon approval of the ANDA.

53. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '404 patent, and that such use in such methods does not require a physician to co-

prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '404 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of Defendants.

54. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and its customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '404 patent. Defendants know or reasonably should know that their proposed conduct will induce infringement.

55. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients

regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with an insulin secretion enhancer, such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '404 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

56. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Defendants' generic pioglitazone-containing drug product.

57. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

58. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '404 patent. Plaintiffs have no adequate remedy at law.

Count IV

(Infringement of the '383 Patent Under 35 U.S.C. § 271(b))

59. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 58 above.

60. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale sale, and/or importation or inducement thereof, of a drug product which is marketed and sold for use in methods claimed in one or more claims of the '383 patent, immediately or imminently upon approval of the ANDA.

61. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '383 patent, and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer such as a sulfonylurea. Further, patients routinely take pioglitazone in combination with additional active

components, such as insulin secretion enhancers for use in methods covered by the '383 patent. The intended use of pioglitazone in combination therapy to treat a glycometabolism disorder, such as diabetes, would be readily apparent to a customer of Defendants.

62. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and its customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '383 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

63. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and

insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with an insulin secretion enhancer such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '383 patent. Defendants know or reasonably should know that their proposed conduct will induce infringement.

64. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphpharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Defendants' generic pioglitazone-containing drug product.

65. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

66. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '383 patent. Plaintiffs have no adequate remedy at law.

Count V

(Infringement of the '042 Patent Under 35 U.S.C. § 271(b))

67. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 66 above.

68. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, sale, and/or importation or inducement thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '042 patent, immediately or imminently upon approval of the ANDA.

69. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '042 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with biguanide, (e.g., metformin). Further, patients routinely take pioglitazone in combination with additional active components, such as

biguanides for use in methods covered by the '042 patent. The intended use of pioglitazone in combination therapy to treat a glycometabolism disorder, such as diabetes, would be readily apparent to a customer of Defendants.

70. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and their customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '042 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

71. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides (e.g., metformin), and that such information will promote the use of

pioglitazone in combination with biguanides. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '042 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

72. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, such as metformin, also applies to Defendants' generic pioglitazone-containing drug product.

73. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

74. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '042 patent. Plaintiffs have no adequate remedy at law.

Count VI

(Infringement of the '043 Patent Under 35 U.S.C. § 271(b))

75. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 74 above.

76. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, sale, and/or importation, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '043 patent, immediately or imminently upon approval of the ANDA.

77. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '043 patents and that use in such methods does not require a physician to co-prescribe pioglitazone with a biguanide, such as metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides for use in methods covered by the '043 patent. The intended use of

pioglitazone in combination therapy to reduce the amount of active components used in such therapy would be readily apparent to a customer of Defendants.

78. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and its customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '043 patent. Defendants know or reasonably should know that their proposed conduct will induce infringement.

79. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides (e.g., metformin), and such information will promote the use of pioglitazone in combination with biguanides. The beneficial effects of such co-administration and/or

interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '043 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

80. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, such as metformin, also applies to Defendants' generic pioglitazone-containing drug product.

81. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

82. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '043 patent. Plaintiffs have no adequate remedy at law.

Count VII

(Infringement of the '090 Patent Under 35 U.S.C. § 271(b))

83. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 82 above.

84. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, and/or sale, or importation thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '090 patent, immediately or imminently upon approval of the ANDA.

85. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '090 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a biguanide, such as metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides for use in methods covered by the '090 patent. The intended use of pioglitazone in combination therapy to reduce side effects of such therapy would be readily apparent to a customer of Defendants.

86. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only

monotherapy. As is well known to Defendants and their customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '090 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

87. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and biguanides (e.g., metformin), and such information will promote the use of pioglitazone in combination with biguanides. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in its label, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '090 patent. Defendants

knows or reasonably should know that their proposed conduct will induce infringement.

88. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and a biguanide, such as metformin, also applies to Defendants' generic pioglitazone-containing drug product.

89. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful. Plaintiffs have no adequate remedy at law.

90. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '090 patent.

Count VIII

(Infringement of the '205 Patent Under 35 U.S.C. § 271(b))

91. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 90 above.

92. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, and/or sale, or importation thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '205 patent, immediately or imminently upon approval of the ANDA.

93. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '205 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '205 patent. The intended use of pioglitazone in combination therapy to reduce the amount of active components used in such therapy would be readily apparent to a customer of Defendants.

94. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and their customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '205 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

95. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and such information will promote the use of pioglitazone in combination with insulin secretion enhancers. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing

pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '205 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

96. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphpharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Defendants' generic pioglitazone-containing drug product.

97. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

98. Plaintiffs will be substantially and irreparably harmed if defendants are not enjoined from inducing the infringement of the '205 patent. Plaintiffs have no adequate remedy at law.

Count IX

(Infringement of the '243 Patent Under 35 U.S.C. § 271(b))

99. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 98 above.

100. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, sale, and/or importation or inducement thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '243 patent, immediately or imminently upon approval of the ANDA.

101. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '243 patents and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin preparation. Further, patients routinely take pioglitazone in combination with additional active components, such as insulin preparations for use in methods covered by the '243 patent. The intended use of pioglitazone in combination therapy to treat a diabetic patient to reduce side effects of active components used in such therapy would be readily apparent to a customer of Defendants.

102. Upon information and belief, Defendants' proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Defendants and their customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '243 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

103. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin preparations and such information will promote the use of pioglitazone in combination with insulin preparations. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be marketing pioglitazone with specific intent,

and/or with the desire to actively induce, aid and abet infringement of the '243 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

104. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin preparation, also applies to Defendants' generic pioglitazone-containing drug product.

105. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

106. Plaintiffs will be substantially and irreparably harmed if defendants are not enjoined from inducing the infringement of the '243 patent.

Count X

(Infringement of the '640 Patent Under 35 U.S.C. § 271(b))

107. Plaintiffs TCI and TPNA repeat and incorporate herein by reference the allegations contained in paragraphs 1 through 106 above.

108. On information and belief, approval of ANDA 76-799 is substantially likely to result in the commercial use, manufacture, offer for sale, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a methods claimed in one or more claims of the '640 patent, immediately or imminently upon approval of the ANDA.

109. Upon information and belief, Defendants are aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '640 patents and that use in such methods does not require a physician to co-prescribe pioglitazone with an insulin secretion enhancer (e.g., a sulfonylurea). Further, patients routinely take pioglitazone in combination with additional active components, such as insulin secretion enhancers for use in methods covered by the '640 patent. The intended use of pioglitazone in combination therapy to reduce side effects of active components used in such therapy would be readily apparent to a customer of Defendants.

110. Upon information and belief, Defendants proposed label for the pioglitazone drug products does not restrict the use of those products to only monotherapy. As well known to Defendants and its customers, the majority of patients treated with pioglitazone take it in combination with another antidiabetic drug, namely, such patients obtain treatment with pioglitazone in combination with a biguanide such as metformin, in combination with an insulin secretion enhancer such as a sulfonylurea, and/or treatment in combination with an insulin preparation. The beneficial effects of such combination therapy are well known to Defendants and customers of Defendants. On information and belief, Defendants will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '640 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

111. Additionally, upon information and belief, Defendants' proposed label also provides, or will be required by the FDA to provide, information for patients regarding the co-administration of, and/or drug interactions between, pioglitazone and insulin secretion enhancers such as a sulfonylurea and that such information will promote the use of pioglitazone in combination with an insulin secretion enhancer. The beneficial effects of such co-administration and/or interactions are well known to customers of Defendants. By including this information in the label, Defendants will be

marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet infringement of the '640 patent. Defendants know or reasonably should know that its proposed conduct will induce infringement.

112. Upon information and belief, Genpharm's generic marketing practices include listing generic products on its website, accessible in the U.S, and promoting these Alphapharm's generic drugs as alternatives to the corresponding brand name pharmaceuticals. Upon information and belief, Genpharm intends to do the same for any approved generic pioglitazone, namely, Genpharm intends to list Alphapharm's generic product and refer consumers to Takeda's product, ACTOS®. Upon information and belief, such marketing practices are substantially likely to lead a consumer of generic pioglitazone to infer that prescribing information for ACTOS®, which includes directions relating to the use of combinations of ACTOS® and an insulin secretion enhancer (e.g., a sulfonylurea), also applies to Defendants' generic pioglitazone-containing drug product.

113. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful.

114. Plaintiffs will be substantially and irreparably harmed if Defendants are not enjoined from inducing the infringement of the '640 patent. Plaintiffs have no adequate remedy at law.

Requested Relief

WHEREFORE, Plaintiffs request the following relief:

(a) a judgment that making, using, selling, offering to sell and/or importing Defendants' drug product for which they seek FDA approval or its active ingredient pioglitazone, and/or inducing the same, will infringe at least one claim of the Takeda Patents;

(b) a judgment that inducing the making, using, offering for sale, selling and/or importing of Defendants' drug product or its active ingredient pioglitazone, and/or inducing the same, will infringe at least one claim of one or more of the Takeda Patents;

(c) a judgment and order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval for Defendants to commercially to make, use, sell, offer to sell or import pioglitazone or any drug product containing pioglitazone be no earlier than the date following the expiration date of the '777 patent;

(d) a permanent injunction restraining and enjoining against any infringement by Defendants, their officers, agents, attorneys, and employees and those acting in privity or concert with it, of the '777

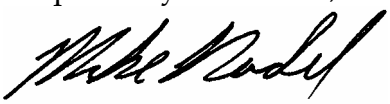
patent or other Takeda Patents through the commercial manufacture, use, sale, offer for sale or importation into the United States of pioglitazone or any drug product containing pioglitazone, and/or any inducement of the same;

(e) Attorneys' fees in this action under 35 U.S.C. § 285;

(f) Such further and other relief as this Court may deem just and proper.

March 16, 2004

Respectfully submitted,



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