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Anthony J. Viola
Andre K. Cizmarik
Zachary W. Silverman
EDWARDS ANGELL PALMER & DODGE LLP
Attorneys for Plaintiffs
Takeda Pharmaceutical Company Limited, and
Takeda Pharmaceuticals North America, Inc.
750 Lexington Ave.
New York, NY 10022
(212) 308-4411

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

Takeda Pharmaceutical Company Limited and Takeda Pharmaceuticals North America, Inc., Plaintiffs, v. Macleods Pharmaceuticals Limited, Defendant.	Civil Action No. _____ COMPLAINT

Plaintiffs, Takeda Pharmaceutical Company Limited (formerly known as Takeda Chemical Industries, Ltd.) ("TPC") and Takeda Pharmaceuticals North America, Inc. ("TPNA") (collectively, "Takeda" or "Plaintiffs"), by their undersigned counsel, for their Complaint against defendant Macleods Pharmaceuticals Limited ("Macleods" or "Defendant"), 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)-(c) and 1400(b). Personal jurisdiction over the defendant in New York is proper under N.Y. C.P.L.R. § 302(a), because it is expected that the defendant will be doing business, and that its actions will have consequences, in this jurisdiction.

Parties

2. TPC 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 American Holdings, Inc., which is a wholly owned U.S. subsidiary of TPC. TPNA has its corporate headquarters and principal place of business in Deerfield, Illinois and is organized under the laws of Delaware.

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

4. On information and belief, Macleods, Inc. is a company organized and existing under the laws of India, having its principal place of business at Atlanta Arcade, Marol Church Road, Andheri (East), Mumbai, India, 400059.

5. Upon information and belief, Macleods filed ANDA No. 202467 (the "Macleods ANDA") with respect to pioglitazone hydrochloride tablets, 15 mg, 30 mg, and 45 mg.

6. Upon information and belief, Macleods intends to sell generic drugs throughout the United States, including in at least New York.

7. Upon information and belief, Macleods intends to transact business in the Southern District of New York, at least by making and shipping into this Judicial District, or by using, offering to sell, or selling, or by causing others to use, offer to sell, or sell, pharmaceutical products, including those referenced in the Macleods ANDA. By filing its ANDA and by its intention to use, offer to sell, sell, or import, or cause others to use, offer to sell, sell, or import, pharmaceutical products, including those referenced in the Macleods ANDA, in the Southern District of New York, Macleods has committed, and unless enjoined, will continue to commit, or will commit, a tortious act without the State of New York, which Macleods expects or should reasonably expect to have consequences in the State of New York, including, but not limited to, causing Takeda's sales of ACTOS® to its New York customers to suffer significantly.

The New Drug Application

8. 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. 21-073).

9. 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® is indicated for monotherapy. ACTOS® is also indicated for use in combination with a sulfonylurea, metformin, or insulin when diet and exercise plus the single agent does not result in adequate glycemic control.

10. 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.

11. Certain amendments to the approved labeling for ACTOS® have subsequently been approved.

The Patents in Suit

12. 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 A**, was duly issued on October 12, 1999 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka and assigned to plaintiff TPC. The '584 patent claims, inter alia, a pharmaceutical composition comprising pioglitazone [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-2,4-thiazolidinedione], 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 a biguanide.

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

14. 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 B**, was duly issued on December 11, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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 glimepiride) and methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin secretion enhancer.

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

16. 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 C**, was duly issued on December 26, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

18. 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 D**, was duly issued on January 9, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

20. 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 E**, was duly issued on April 3, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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).

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

22. 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 F**, was duly issued on August 7, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

24. 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 G**, was duly issued on October 16, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '640 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 a pioglitazone or salt thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

25. Plaintiff TPC has been and still is the owner through assignment of the '640 patent, which expires on August 9, 2016.

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

27. In accordance with its exclusive license, plaintiff TPNA sells pioglitazone-containing drug products under the trade name ACTOS®, among others, in the United States. Sales of TPNA's pioglitazone-containing drug products are made pursuant to approval by the FDA of, among others, NDA No. 21-073.

28. Plaintiff TPC manufactures the ACTOS® drug products sold by TPNA.

29. Plaintiffs TPC 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

(INFRINGEMENT OF THE '584 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

30. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

31. Upon information and belief, Macleods filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j) (ANDA No. 202467) seeking approval to market 15 mg, 30 mg, and 45 mg tablets comprising pioglitazone as its hydrochloride ("HCl") salt.

32. By this ANDA filing, Macleods has indicated that it intends to engage, and that there is substantial likelihood that it will engage, in the commercial manufacture, importation, use, offer for sale, and/or sale, or inducement thereof, of plaintiffs' patented pioglitazone drug products immediately or imminently upon receiving FDA approval to do so. Also by its ANDA

filing, Macleods has indicated that its drug products containing pioglitazone are bioequivalent to Takeda's pioglitazone drug products.

33. By its ANDA filing, Macleods seeks to obtain approval to commercially manufacture, use, import, offer for sale, and/or sell, alleged generic equivalents of plaintiffs' ACTOS® pioglitazone drug products prior to the expiration date of the '584 patent.

34. By a letter (the "Notice Letter") dated April 18, 2010, Macleods informed TPC and TPNA that Macleods had filed a certification to the FDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). On or about April 19, 2011, NDA holder, TPNA, received the Notice Letter. On or about April 22, 2011, patent owner, TPC, received a duplicate original of the Notice Letter.

35. The Notice Letter, purporting to be Macleods's Notice of Certification under 21 U.S.C. § 355(j)(2)(B)(ii), indicates that Macleods intends to manufacture, use or sell pioglitazone hydrochloride tablets before the expiration of the '584 patent. The Notice Letter states that "in its opinion and to the best of its knowledge, each claim of [the '584 patent] . . . is invalid and/or will not be infringed by the commercial manufacture, use or sale of the drug product described by Macleods' ANDA."

36. Macleods's filing of ANDA No. 202467 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, importation, offer for sale and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '584 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

37. Macleods's manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of its proposed pioglitazone drug product will induce infringement of at least one claim of the '584 patent under 35 U.S.C. § 271(e)(2)(A).

38. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy, and that such use does not require a physician to co-prescribe pioglitazone with a biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to customers of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

39. Upon information and belief, Macleods currently manufactures, markets, and/or sells the biguanide, metformin.

40. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

41. Additionally, upon information and belief, Macleods's 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, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

42. Upon information and belief, Macleods has planned and intended to actively induce others to infringe the '584 patent when its ANDA application is approved and plans and intends to do so on approval.

43. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '584 patent.

44. Unless Macleods is enjoined from infringing and inducing the infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT II

(INFRINGEMENT OF THE '404 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

45. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

46. The Macleods Notice Letter also indicates that Macleods intends to manufacture, use, or sell pioglitazone hydrochloride tablets before the expiration of the '404 patent. The Notice Letter states that ""in its opinion and to the best of its knowledge, each claim of [the '404 patent]. . . is invalid and/or will not be infringed by the commercial manufacture, use or sale of the drug product described by Macleods' ANDA."

47. Macleods's filing of ANDA No. 202467 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, importation, offer for sale and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '404 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

48. Macleods's manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of its proposed pioglitazone drug product will induce infringement of at least one claim of the '404 patent under 35 U.S.C. § 271(e)(2)(A).

49. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy, and that such use 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. The intended use of pioglitazone in combination therapy would be readily apparent to customers of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

50. Upon information and belief, Macleods currently manufactures, markets, and/or sells the insulin secretion enhancer, glimepiride.

51. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

52. Additionally, upon information and belief, Macleods's 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 such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

53. Upon information and belief, Macleods has planned and intended to actively induce others to infringe the '404 patent when its ANDA application is approved and plans and intends to do so on approval.

54. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '404 patent.

57. Unless Macleods is enjoined from infringing and inducing the infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT III

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '584 PATENT UNDER 35 U.S.C. § 271(b))

58. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

59. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale, and/or sale, 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 '584 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '584 patent.

60. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '584 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a 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 '584 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

61. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

62. Additionally, upon information and belief, Macleods's 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 biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

64. Unless Macleods is enjoined from infringing and inducing infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IV

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '404 PATENT UNDER 35 U.S.C. § 271(b))

65. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

66. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in the '404 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '404 patent.

67. Upon information and belief, Macleods is 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 use in such method 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

68. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific

intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

69. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

71. Unless Macleods is enjoined from infringing and inducing infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT V

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '043 PATENT UNDER 35 U.S.C. § 271(b))

72. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

73. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale, 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, and prior to the expiration of the '043 patent.

74. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '043 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a 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 '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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

75. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

76. Additionally, upon information and belief, Macleods's 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, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

78. Unless Macleods is enjoined from infringing and inducing infringement of the '043 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VI

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '090 PATENT UNDER 35 U.S.C. § 271(b))

79. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

80. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '090 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '090 patent.

81. Upon information and belief, Macleods is 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, e.g., 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

82. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

83. Additionally, upon information and belief, Macleods's 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, e.g.,

metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

85. Unless Macleods is enjoined from infringing and inducing infringement of the '090 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '205 PATENT UNDER 35 U.S.C. § 271(b))

86. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

87. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale, 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 '205 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '205 patent.

88. Upon information and belief, Macleods is 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

89. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '205 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

90. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively

induce, aid and abet, infringement of the '205 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

92. Unless Macleods is enjoined from infringing and inducing infringement of the '205 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VIII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '243 PATENT UNDER 35 U.S.C. § 271(b))

93. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

94. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, 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 '243 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '243 patent.

95. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '243 patent 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

Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

96. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

97. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

99. Unless Macleods is enjoined from infringing and inducing infringement of the '243 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IX

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '640 PATENT UNDER 35 U.S.C. § 271(b))

100. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

101. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, 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, and prior to the expiration of the '640 patent.

102. Upon information and belief, Macleods is 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy

benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

103. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

104. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

106. Unless Macleods is enjoined from infringing and inducing infringement of the '640 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

WHEREFORE, Plaintiffs request the following relief:

(a) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that making, using, selling, offering to sell and/or importing Macleods's drug product for which it seeks FDA approval or its active ingredient pioglitazone will infringe at least one claim of one or more of the Takeda Patents;

(b) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that inducing the making, using, offering for sale, selling and/or importing of Macleods's drug product or its active ingredient pioglitazone, will infringe at least one claim of one or more of the Takeda Patents;

(c) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. and an order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval for Macleods to commercially 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 last to expire of the Takeda Patents (as extended, if applicable);

(d) a permanent injunction restraining and enjoining against any infringement by defendants, their officers, agents, attorneys, employees, successors or assigns, or those acting in privity or concert with them, of the 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; and

(f) Such further and other relief in favor of Plaintiffs and against Defendants as this Court may deem just and proper.

Dated: New York, New York
May 6, 2011

Takeda Pharmaceutical Company Limited and
Takeda Pharmaceuticals North America, Inc.

By their attorneys,

Anthony J. Viola
Andre K. Cizmarik
Zachary W. Silverman
EDWARDS ANGELL PALMER & DODGE LLP
750 Lexington Avenue
New York, NY 10022
(212) 308-4411

David G. Conlin (to be admitted *pro hac vice*)
Barbara L. Moore (to be admitted *pro hac vice*)
Kathleen B. Carr (to be admitted *pro hac vice*)
Adam P. Samansky (to be admitted *pro hac vice*)
EDWARDS ANGELL PALMER & DODGE LLP
111 Huntington Avenue
Boston, MA 02199-7613
(617) 239-0100

11. Certain amendments to the approved labeling for ACTOS® have subsequently been approved.

The Patents in Suit

12. 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 A**, was duly issued on October 12, 1999 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka and assigned to plaintiff TPC. The '584 patent claims, inter alia, a pharmaceutical composition comprising pioglitazone [(±)-5-[[4-[2-(5-ethyl-2-pyridinyl)ethoxy]phenyl]methyl]-2,4-thiazolidinedione], 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 a biguanide.

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

14. 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 B**, was duly issued on December 11, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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 glimepiride) and methods for treating diabetes which comprise administering a therapeutically effective amount of pioglitazone or salts thereof in combination with an insulin secretion enhancer.

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

16. 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 C**, was duly issued on December 26, 2000 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

18. 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 D**, was duly issued on January 9, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

20. 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 E**, was duly issued on April 3, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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).

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

22. 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 F**, was duly issued on August 7, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. 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.

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

24. 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 G**, was duly issued on October 16, 2001 to inventors Hitoshi Ikeda, Takashi Sohda and Hiroyuki Odaka, and assigned to plaintiff TPC. The '640 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 a pioglitazone or salt thereof in combination with an insulin secretion enhancer (e.g., a sulfonylurea).

25. Plaintiff TPC has been and still is the owner through assignment of the '640 patent, which expires on August 9, 2016.

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

27. In accordance with its exclusive license, plaintiff TPNA sells pioglitazone-containing drug products under the trade name ACTOS®, among others, in the United States. Sales of TPNA's pioglitazone-containing drug products are made pursuant to approval by the FDA of, among others, NDA No. 21-073.

28. Plaintiff TPC manufactures the ACTOS® drug products sold by TPNA.

29. Plaintiffs TPC 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

(INFRINGEMENT OF THE '584 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

30. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

31. Upon information and belief, Macleods filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j) (ANDA No. 202467) seeking approval to market 15 mg, 30 mg, and 45 mg tablets comprising pioglitazone as its hydrochloride ("HCl") salt.

32. By this ANDA filing, Macleods has indicated that it intends to engage, and that there is substantial likelihood that it will engage, in the commercial manufacture, importation, use, offer for sale, and/or sale, or inducement thereof, of plaintiffs' patented pioglitazone drug products immediately or imminently upon receiving FDA approval to do so. Also by its ANDA

filing, Macleods has indicated that its drug products containing pioglitazone are bioequivalent to Takeda's pioglitazone drug products.

33. By its ANDA filing, Macleods seeks to obtain approval to commercially manufacture, use, import, offer for sale, and/or sell, alleged generic equivalents of plaintiffs' ACTOS® pioglitazone drug products prior to the expiration date of the '584 patent.

34. By a letter (the "Notice Letter") dated April 18, 2010, Macleods informed TPC and TPNA that Macleods had filed a certification to the FDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). On or about April 19, 2011, NDA holder, TPNA, received the Notice Letter. On or about April 22, 2011, patent owner, TPC, received a duplicate original of the Notice Letter.

35. The Notice Letter, purporting to be Macleods's Notice of Certification under 21 U.S.C. § 355(j)(2)(B)(ii), indicates that Macleods intends to manufacture, use or sell pioglitazone hydrochloride tablets before the expiration of the '584 patent. The Notice Letter states that "in its opinion and to the best of its knowledge, each claim of [the '584 patent] . . . is invalid and/or will not be infringed by the commercial manufacture, use or sale of the drug product described by Macleods' ANDA."

36. Macleods's filing of ANDA No. 202467 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, importation, offer for sale and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '584 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

37. Macleods's manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of its proposed pioglitazone drug product will induce infringement of at least one claim of the '584 patent under 35 U.S.C. § 271(e)(2)(A).

38. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy, and that such use does not require a physician to co-prescribe pioglitazone with a biguanide, e.g., metformin. Further, patients routinely take pioglitazone in combination with additional active components, such as biguanides. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to customers of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

39. Upon information and belief, Macleods currently manufactures, markets, and/or sells the biguanide, metformin.

40. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

41. Additionally, upon information and belief, Macleods's 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, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

42. Upon information and belief, Macleods has planned and intended to actively induce others to infringe the '584 patent when its ANDA application is approved and plans and intends to do so on approval.

43. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '584 patent.

44. Unless Macleods is enjoined from infringing and inducing the infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT II

(INFRINGEMENT OF THE '404 PATENT UNDER 35 U.S.C. § 271(E)(2)(A))

45. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

46. The Macleods Notice Letter also indicates that Macleods intends to manufacture, use, or sell pioglitazone hydrochloride tablets before the expiration of the '404 patent. The Notice Letter states that ""in its opinion and to the best of its knowledge, each claim of [the '404 patent]. . . is invalid and/or will not be infringed by the commercial manufacture, use or sale of the drug product described by Macleods' ANDA."

47. Macleods's filing of ANDA No. 202467 for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, importation, offer for sale and/or sale, or inducement thereof, of drug products containing pioglitazone or salts thereof before the expiration of the '404 patent is an act of infringement under 35 U.S.C. § 271(e)(2)(A).

48. Macleods's manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of its proposed pioglitazone drug product will induce infringement of at least one claim of the '404 patent under 35 U.S.C. § 271(e)(2)(A).

49. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in combination therapy, and that such use 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. The intended use of pioglitazone in combination therapy would be readily apparent to customers of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

50. Upon information and belief, Macleods currently manufactures, markets, and/or sells the insulin secretion enhancer, glimepiride.

51. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

52. Additionally, upon information and belief, Macleods's 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 such as a sulfonylurea. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

53. Upon information and belief, Macleods has planned and intended to actively induce others to infringe the '404 patent when its ANDA application is approved and plans and intends to do so on approval.

54. Upon information and belief, the acts of infringement alleged above are and have been deliberate and willful, and in full knowledge of the existence of the '404 patent.

57. Unless Macleods is enjoined from infringing and inducing the infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT III

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '584 PATENT UNDER 35 U.S.C. § 271(b))

58. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

59. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale, and/or sale, 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 '584 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '584 patent.

60. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '584 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a 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 '584 patent. The intended use of pioglitazone in combination therapy to treat diabetes would be readily apparent to a customer of Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

61. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

62. Additionally, upon information and belief, Macleods's 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 biguanides, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '584 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

64. Unless Macleods is enjoined from infringing and inducing infringement of the '584 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IV

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '404 PATENT UNDER 35 U.S.C. § 271(b))

65. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

66. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale, and/or sale, or inducement thereof, of a drug product which is marketed and sold for use in a method claimed in the '404 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '404 patent.

67. Upon information and belief, Macleods is 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 use in such method 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

68. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific

intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

69. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '404 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

71. Unless Macleods is enjoined from infringing and inducing infringement of the '404 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT V

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '043 PATENT UNDER 35 U.S.C. § 271(b))

72. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

73. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale, 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, and prior to the expiration of the '043 patent.

74. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '043 patent and that use in such methods does not require a physician to co-prescribe pioglitazone with a 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 '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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

75. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

76. Additionally, upon information and belief, Macleods's 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, e.g., metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '043 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

78. Unless Macleods is enjoined from infringing and inducing infringement of the '043 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VI

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '090 PATENT UNDER 35 U.S.C. § 271(b))

79. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

80. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale of a drug product which is marketed and sold for use in a method claimed in one or more claims of the '090 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '090 patent.

81. Upon information and belief, Macleods is 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, e.g., 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

82. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

83. Additionally, upon information and belief, Macleods's 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, e.g.,

metformin. The beneficial effects of such co-administration and/or interactions are well known to customers of Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '090 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

85. Unless Macleods is enjoined from infringing and inducing infringement of the '090 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '205 PATENT UNDER 35 U.S.C. § 271(b))

86. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

87. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, offer for sale and/or sale, 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 '205 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '205 patent.

88. Upon information and belief, Macleods is 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

89. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '205 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

90. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively

induce, aid and abet, infringement of the '205 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

92. Unless Macleods is enjoined from infringing and inducing infringement of the '205 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VIII

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '243 PATENT UNDER 35 U.S.C. § 271(b))

93. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

94. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, 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 '243 patent, immediately or imminently upon approval of the ANDA, and prior to the expiration of the '243 patent.

95. Upon information and belief, Macleods is aware or reasonably should be aware, of the widespread use of pioglitazone in the methods of one or more claims of the '243 patent 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

Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

96. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

97. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '243 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

99. Unless Macleods is enjoined from infringing and inducing infringement of the '243 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IX

(INFRINGEMENT OF THE METHOD CLAIMS OF THE '640 PATENT UNDER 35 U.S.C. § 271(b))

100. Plaintiffs TPC and TPNA repeat and incorporate herein by reference the allegations contained in each of the foregoing paragraphs.

101. Upon information and belief, approval of ANDA 202467 is substantially likely to result in the commercial manufacture, use, importation, 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, and prior to the expiration of the '640 patent.

102. Upon information and belief, Macleods is 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 Macleods (e.g., including, without limitation, physicians, pharmacists, pharmacy

benefits management companies, health care providers who establish drug formularies for their insurers and/or patients).

103. Upon information and belief, Macleods's proposed label for its pioglitazone drug products does not restrict the use of those products to only monotherapy. As is well known to Macleods 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 Macleods and customers of Macleods. On information and belief, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

104. Additionally, upon information and belief, Macleods's 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 Macleods. By including this information in its label, Macleods will be marketing pioglitazone with specific intent, and/or with the desire to actively induce, aid and abet, infringement of the '640 patent. Macleods knows or reasonably should know that its proposed conduct will induce infringement.

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

106. Unless Macleods is enjoined from infringing and inducing infringement of the '640 patent, plaintiffs will suffer substantial and irreparable injury. Plaintiffs have no adequate remedy at law.

WHEREFORE, Plaintiffs request the following relief:

(a) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that making, using, selling, offering to sell and/or importing Macleods's drug product for which it seeks FDA approval or its active ingredient pioglitazone will infringe at least one claim of one or more of the Takeda Patents;

(b) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. that inducing the making, using, offering for sale, selling and/or importing of Macleods's drug product or its active ingredient pioglitazone, will infringe at least one claim of one or more of the Takeda Patents;

(c) a declaratory judgment pursuant to 28 U.S.C. § 2201 et seq. and an order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval for Macleods to commercially 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 last to expire of the Takeda Patents (as extended, if applicable);

(d) a permanent injunction restraining and enjoining against any infringement by defendants, their officers, agents, attorneys, employees, successors or assigns, or those acting in privity or concert with them, of the 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; and

(f) Such further and other relief in favor of Plaintiffs and against Defendants as this Court may deem just and proper.

Dated: New York, New York
May 6, 2011

Takeda Pharmaceutical Company Limited and
Takeda Pharmaceuticals North America, Inc.

By their attorneys,

Anthony J. Viola
Andre K. Cizmarik
Zachary W. Silverman
EDWARDS ANGELL PALMER & DODGE LLP
750 Lexington Avenue
New York, NY 10022
(212) 308-4411

David G. Conlin (to be admitted *pro hac vice*)
Barbara L. Moore (to be admitted *pro hac vice*)
Kathleen B. Carr (to be admitted *pro hac vice*)
Adam P. Samansky (to be admitted *pro hac vice*)
EDWARDS ANGELL PALMER & DODGE LLP
111 Huntington Avenue
Boston, MA 02199-7613
(617) 239-0100