IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. ALKEM LABORATORIES LIMITED and ASCEND LABORATORIES, LLC, Defendants.	C.A. No. _____ [redacted] **PUBLIC VERSION**

COMPLAINT

Plaintiff Takeda Pharmaceuticals U.S.A., Inc. ("Takeda" or "Plaintiff"), by their undersigned attorneys, for their Complaint against Alkem Laboratories Limited and Ascend Laboratories, LLC (collectively, "Alkem"), herein allege as follows:

NATURE OF THE ACTION

1. Takeda brings this civil action against Alkem for breach of the License Agreement[1], attached hereto as Exhibit A, under Delaware law, and for patent infringement under the patent laws of the United States, Title 35, United States Code, involving United States Patent Nos. 7,906,519 ("the '519 patent"); 7,935,731 ("the '731 patent"); 8,093,298 ("the '298 patent") (*infra* ¶ 44); 7,964,648 ("the '648 patent"); 8,093,297 ("the '297 patent"); 7,619,004 ("the '004 patent"); 7,601,758 ("the '758 patent"); 7,820,681 ("the '681 patent"); 7,915,269

[1] Exhibit A includes both the Settlement Agreement and the License Agreement. The License Agreement was executed contemporaneously along with and as a part of the Settlement Agreement by Takeda and Alkem on May 23, 2018. The Settlement and License Agreements contain confidential information such as specific dates and time spans with respect to Generic Entry Dates.

("the '269 patent"); 7,964,647 ("the '647 patent"); 7,981,938 ("the '938 patent"); 8,093,296 ("the '296 patent"); 8,097,655 ("the '655 patent"); 8,415,395 ("the '395 patent"); 8,415,396 ("the '396 patent"); 8,440,721 ("the '721 patent"); and 8,440,722 ("the '722 patent") (*infra* ¶ 45) (collectively, the "Patents-in-Suit").

THE PARTIES

2. Plaintiff Takeda Pharmaceuticals U.S.A., Inc. is a corporation organized and existing under the laws of the State of Delaware, and its principal place of business is located at One Takeda Parkway, Deerfield, Illinois 60015.

3. Upon information and belief, defendant Alkem Laboratories Limited ("Alkem Laboratories") is a corporation organized and existing under the laws of the Republic of India, and its principal place of business is located at Devashish Building, Alkem House, Senpati Bapat Road, Lower Parel, Mumbai 400013, Maharashtra, India.

4. Upon information and belief, defendant Ascend Laboratories, LLC ("Ascend Laboratories") is a wholly owned subsidiary of Alkem Laboratories. Ascend Laboratories is a corporation organized and existing under the laws of the State of New Jersey, and its principal place of business is located at 339 Jefferson Road, Suite 101, Parsippany, New Jersey 07054.

5. Upon information and belief, Ascend Laboratories is an agent or affiliate of Alkem Laboratories and is acting as the agent of Alkem Laboratories with respect to ANDA No. 211250.

6. Upon information and belief, Ascend Laboratories markets, distributes, sells, and/or offers for sale generic drugs throughout the United States and in Delaware at the direction of, under the control of, in concert with, and for the direct benefit of Alkem Laboratories.

7. Upon information and belief, Ascend Laboratories is an agent or affiliate of Alkem Laboratories and is acting at the direction of, under the control of, in concert with, and for the direct benefit of Alkem Laboratories.

8. Upon information and belief, Alkem Laboratories and Ascend Laboratories will act in concert to market, distribute, offer for sale, and sell the Alkem ANDA Product (*infra* ¶ 53) throughout the United States and within Delaware.

JURISDICTION AND VENUE

9. This Court has subject-matter jurisdiction over this action with respect to the patent-infringement claims pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202 because this action arises under the patent laws of the United States and seeks relief under the Federal Declaratory Judgment Act.

10. This Court has subject-matter jurisdiction over the breach-of-contract claim pursuant to 28 U.S.C. § 1332(a) because there is complete diversity between the parties and the amount in controversy exceeds $75,000.

11. This Court also has subject-matter jurisdiction over the breach-of-contract claim pursuant to 28 U.S.C. § 1367(a).

12. This Court has subject-matter jurisdiction over this action pursuant to this Court's July 6, 2018 Order in *Takeda Pharmaceuticals U.S.A., Inc. v. Alkem Laboratories Ltd. and Ascend Laboratories LLC.*, C.A. No. 18-cv-189-RGA (D. Del.) (D.I. 16) ("Order," which is attached as Exhibit B and is incorporated herein by reference as though set forth in full, in which this Court retained jurisdiction to enforce the parties' settlement agreement) (Ex. B, Order at ¶ 2).

13. Alkem expressly consented and submitted itself to personal jurisdiction in this District in Section 5 of the License Agreement. (Ex. A, License Agr't § 5).

14. Venue is proper under 28 U.S.C. § 1391(b) and (c) because, among other reasons, Alkem consented to venue in this District as part of the License Agreement. (Ex. A, License Agr't § 5).

15. Upon information and belief, the Alkem ANDA Product will, among other things, be marketed and distributed in Delaware, and/or prescribed by physicians practicing in Delaware and dispensed by pharmacies located within Delaware, all of which will have a substantial effect on Delaware. Upon information and belief, Alkem intends that the Alkem ANDA Product will be distributed and sold in the United States, including in Delaware. If Ascend Laboratories is permitted to market the Alkem ANDA Product, Takeda will be specifically harmed by Ascend Laboratories's sales of the Alkem ANDA Product, including its sales in Delaware.

16. Upon information and belief, Alkem has engaged in pre-booking activities of the Alkem ANDA Product having at least had discussions with [redacted].

BACKGROUND FACTS

A. Takeda's Colcrys® Product

17. Colcrys® (colchicine, USP) tablets, 0.6 mg is approved by the FDA for the treatment of familial Mediterranean fever ("FMF") in adults and children 4 years or older, and the prophylaxis and treatment of gout flares in adults.

18. FMF is a rare inherited disease characterized by abdominal pain and significant morbidity.

19. Gout is an extremely painful rheumatologic condition characterized by chronic manifestations and acute flares, which are often caused by the accumulation of uric acid.

20. Colcrys® was the first pharmaceutical product approved by the United States Food and Drug Administration ("FDA") that contained colchicine as the sole active ingredient. While colchicine had been used in the United States for many years before the approval of Colcrys®, use of single-ingredient colchicine was not approved by the FDA.

21. In 2006, the FDA encouraged the pharmaceutical industry to submit a New Drug Applications ("NDA") for previously unapproved drugs in order for the FDA to substantively evaluate older drug products by modern standards.

22. Mutual Pharmaceutical Company, Inc. ("Mutual") sponsored a clinical study that revealed important new information about colchicine administration. The study revealed that a substantially lower total dose of colchicine was effective to treat gout flares compared to the previous standard of care dose, resulting in significantly fewer adverse events. The study also identified potentially lethal interactions between certain classes of drugs and colchicine.

23. Mutual submitted NDAs for single-ingredient colchicine tablets under Section 505(b)(2) of the Federal Food, Drug and Consumer Act. Mutual submitted: (1) NDA No. 22-351 for the treatment of acute gout, (2) NDA No. 22-352 for the treatment of FMF, and (3) NDA No. 22-353 for the prevention of gout flares in the chronic treatment of gout.

24. FDA approved NDA No. 22-352 on July 29, 2009. FDA approved NDA No. 22-351 on July 30, 2009. FDA approved NDA No. 22-353 on October 16, 2009.

25. Takeda is currently the holder of NDA Nos. 22-351, 22-352, and 22-353.

B. Takeda's Colcrys® Patents

26. Takeda is the lawful owner of all right, title, and interest in and to the following United States patents set forth in paragraphs 27-43 below, including the right to sue and to recover for infringement thereof, which contain one or more claims covering methods of using Colcrys®.

27. The ’519 patent, titled “Methods for Concomitant Administration of Colchicine and a Second Active Agent,” a copy of which is attached hereto as Exhibit C and incorporated herein by reference as though set forth in full, was duly and legally issued March 15, 2011, naming Matthew W. Davis as the inventor. The ’519 patent claims, *inter alia*, a method of treating a patient with familial Mediterranean fever with colchicine by orally administering an adjusted daily dosage amount of colchicine wherein the patient is receiving concomitant administration of ritonavir.

28. The ’731 patent, titled “Methods For Concomitant Administration of Colchicine and Macrolide Antibiotics,” a copy of which is attached hereto as Exhibit D and incorporated herein by reference as though set forth in full, was duly and legally issued May 3, 2011, naming Matthew W. Davis as the inventor. The ’731 patent claims, *inter alia*, a method of using colchicine for the treatment of familial Mediterranean fever comprising orally administering a reduced colchicine dosage amount to a patient who is concomitantly receiving clarithromycin.

29. The ’298 patent, titled “Methods for Concomitant Administration of Colchicine and Macrolide Antibiotics,” a copy of which is attached hereto as Exhibit E and incorporated herein by reference as though set forth in full, was duly and legally issued January 10, 2012, naming Matthew W. Davis as the inventor. The ’298 patent claims, *inter alia*, a method of using colchicine for the treatment of familial Mediterranean fever by orally administering a reduced dosage amount of colchicine to a adult or child who is concomitantly receiving clarithromycin.

30. The ’648 patent, titled “Methods for Concomitant Administration of Colchicine and a Second Active Agent,” a copy of which is attached hereto as Exhibit F and incorporated herein by reference as though set forth in full, was duly and legally issued June 21, 2011,

naming Matthew W. Davis as the inventor. The '648 patent claims, *inter alia*, a method of treating a patient with familial Mediterranean fever or gout with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine to the patient who is receiving concomitant administration of ketoconazole.

31. The '297 patent, titled "Methods for Concomitant Administration of Colchicine and a Second Active Agent," a copy of which is attached hereto as Exhibit G and incorporated herein by reference as though set forth in full, was duly and legally issued January 10, 2012, naming Matthew W. Davis as the inventor. The '297 patent claims, *inter alia*, a method of treating a patient in need of treatment for familial Mediterranean fever or gout with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine to the patient who is receiving concomitant administration of a recommended daily dosage amount of ritonavir.

32. The '004 patent, titled "Methods for Concomitant Administration of Colchicine and Macrolide Antibiotics," a copy of which is attached hereto as Exhibit H and incorporated herein by reference as though set forth in full, was duly and legally issued November 17, 2009, naming Matthew W. Davis as the inventor. The '004 patent claims, *inter alia*, a method of using colchicine for prophylactic treatment of gout flares in a human gout patient so as to reduce the occurrence of colchicine toxicity when said patient is receiving concomitant administration of clarithromycin.

33. The '758 patent, titled "Methods for Concomitant Administration of Colchicine and Macrolide Antibiotics in the Treatment of Gout Flares," a copy of which is attached hereto as Exhibit I and incorporated herein by reference as though set forth in full, was duly and legally issued October 13, 2009, naming Matthew W. Davis as the inventor. The '758 patent

claims, *inter alia*, a method of using colchicine to treat a gout flare in a human patient who is receiving concomitant administration of clarithromycin or erythromycin.

34. The ’681 patent, titled “Methods for Concomitant Administration of Colchicine and a Second Active Agent,” a copy of which is attached hereto as Exhibit J and incorporated herein by reference as though set forth in full, was duly and legally issued October 26, 2010, naming Matthew W. Davis as the inventor. The ’681 patent claims, *inter alia*, a method of treating a patient in need of treatment for the prophylaxis of gout flares with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine to a patient who is receiving concomitant administration of ritonavir.

35. The ’269 patent, titled “Methods for Concomitant Administration of Colchicine and a Second Active Agent,” a copy of which is attached hereto as Exhibit K and incorporated herein by reference as though set forth in full, was duly and legally issued March 29, 2011, naming Matthew W. Davis as the inventor. The ’269 patent claims, *inter alia*, a method of treating a patient in need of treatment for gout flares with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine wherein the patient is receiving concomitant administration of ritonavir.

36. The ’647 patent, titled “Colchicine Compositions and Methods,” a copy of which is attached hereto as Exhibit L and incorporated herein by reference as though set forth in full, was duly and legally issued June 21, 2011, naming Matthew W. Davis as the inventor. The ’647 patent claims, *inter alia*, a method of treating a patient having an acute gouty arthritis attack with colchicine.

37. The ’938 patent, titled “Colchicine Compositions and Methods,” a copy of which is attached hereto as Exhibit M and incorporated herein by reference as though set forth in full,

was duly and legally issued July 19, 2011, naming Matthew W. Davis as the inventor. The ’938 patent claims, *inter alia*, a method of treating a gout flare with colchicine in a patient undergoing colchicine prophylactic treatment of gout flares.

38. The ’296 patent, titled “Methods for Concomitant Administration of Colchicine and Macrolide Antibiotics,” a copy of which is attached hereto as Exhibit N and incorporated herein by reference as though set forth in full, was duly and legally issued January 10, 2012, naming Matthew W. Davis as the inventor. The ’296 patent claims, *inter alia*, a method of using colchicine to treat gout flares in an adult human gout patient so as to reduce the occurrence of colchicine toxicity when the patient is receiving concomitant administration of clarithromycin.

39. The ’655 patent, titled “Methods for Concomitant Administration of Colchicine and Macrolide Antibiotics,” a copy of which is attached hereto as Exhibit O and incorporated herein by reference as though set forth in full, was duly and legally issued January 17, 2012, naming Matthew W. Davis as the inventor. The ’655 patent claims, *inter alia*, a method of using colchicine for prophylactic treatment of gout flares in an adult human gout patient so as to reduce the occurrence of colchicine toxicity when said patient is receiving concomitant administration of clarithromycin.

40. The ’395 patent, titled “Colchicine Compositions and Methods,” a copy of which is attached hereto as Exhibit P and incorporated herein by reference as though set forth in full, was duly and legally issued April 9, 2013, naming Matthew W. Davis and Hengsheng Feng as inventors. The ’395 patent claims, *inter alia*, a method of treating a patient having a gout flare.

41. The ’396 patent, titled “Colchicine Compositions and Methods,” a copy of which is attached hereto as Exhibit Q and incorporated herein by reference as though set forth in full,

was duly and legally issued April 9, 2013, naming Matthew W. Davis and Hengsheng Feng as inventors. The '396 patent claims, *inter alia*, a method of treating a patient having a gout flare.

42. The '721 patent, titled "Methods for Concomitant Administration of Colchicine and a Second Active Agent," a copy of which is attached hereto as Exhibit R and incorporated herein by reference as though set forth in full, was duly and legally issued May 14, 2013, naming Matthew W. Davis as the inventor. The '721 patent claims, *inter alia*, a method of treating a patient in need of treatment for acute gout flares with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine to the patient who is receiving concomitant administration of verapamil.

43. The '722 patent, titled "Methods for Concomitant Administration of Colchicine and a Second Active Agent," a copy of which is attached hereto as Exhibit S and incorporated herein by reference as though set forth in full, was duly and legally issued May 14, 2013, naming Matthew W. Davis as the inventor. The '722 patent claims, *inter alia*, a method of treating a patient in need of treatment for prophylaxis of gout flares with colchicine, comprising orally administering an adjusted daily dosage amount of colchicine to the patient who is receiving concomitant administration of verapamil.

44. The '519, '731, '298, '648 and '297 patents are collectively referred to herein as the "FMF Patents."

45. The '004, '758, '681, '269, '647, '648, '938, '296, '297, '655, '395, '396, '721, and '722 patents are collectively referred to herein as the "Gout Patents." (The '648 and '297 patents are both FMF Patents and Gout Patents).

46. Pursuant to 21 U.S.C. § 355(b)(1), the Patents-in-Suit are listed in the FDA's publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book") as covering Colcrys®.

C. The Gout and FMF Markets in the United States

47. Colcrys® is predominantly used as a medication for treating or preventing gout flares. According to the National Health and Nutrition Examination Survey, between 2015-2016, 9.2 million people in the United States suffered from gout. (Ex. T, NHANES Data).

48. Upon information and belief, the Alkem ANDA (*infra* ¶ 53) has been approved by the FDA to sell generic colchicine tablets solely for the FMF indication, and not for the prophylaxis or treatment of gout in adults. The National Institute of Health Office of Rare Diseases classifies FMF as a "rare disease" with fewer than 200,000 affected individuals in the United States.

49. According to national prescription data from inVentiv Health (formerly Encuity Research), for the fifteen-year period between August 2001 and August 2016, only approximately 32,000 colchicine prescriptions were written for FMF patients in the United States (*i.e.*, only 2,133 prescriptions per year for FMF, compared to 913,000 prescriptions per year for gout). According to this national prescription data, less than one percent (0.21%) (or approximately 1 in 472) of colchicine prescription were for FMF. And among prescriptions written for FDA-approved uses for colchicine—gout and FMF—approximately 0.23% (or approximately 1 in 449) of the prescriptions were for FMF, while approximately 99.77% of the prescriptions were for gout.

50. Upon information and belief, Alkem intends to manufacture the Alkem ANDA Product in quantities that far exceed the available market for the treatment of FMF in the United States.

D. Physician Prescribing Practices and Pharmacy Dispensing Practices

51. Physicians make prescribing decisions for medication based on their knowledge, experience, training, and review of medical literature, including the Physicians' Desk Reference and the package insert or "label." However, physicians typically do not control whether a pharmacist fills a prescription with a brand drug or with any particular generic version. The majority of states allow pharmacists to substitute generic drugs for brand name drugs so long as the patient approves. Indeed, in fifteen states, substitution of the generic version of a drug is mandatory. *See* 2016 National Association of Boards of Pharmacy (NABP) Survey of Pharmacy Law at 71-74 (attached hereto as Exhibit U) (reporting that fifteen states require "mandatory" generic substitution and that forty-nine states permit substitution without permission from the prescriber or purchaser). Thus, where a generic version of a brand drug exists, pharmacists regularly will substitute the generic drug for the brand, regardless of whether the generic drug is FDA-approved for the indication for which the brand drug was prescribed.

52. Upon information and belief, even if Ascend Laboratories markets the Alkem ANDA Product with a label containing only an FMF indication, prescriptions written for "Colcrys®" and "colchicine" for the treatment and/or prevention of gout flares will be filled with the Alkem ANDA Product.

E. Previous Colcrys® Litigation with Alkem, C.A. No. 18-cv-189-RGA (D. Del.)

53. In 2017, Alkem Laboratories submitted Abbreviated New Drug Application ("ANDA") No. 211250 to the FDA ("Alkem ANDA"), seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of generic 0.6 mg oral colchicine tablets—a generic version of Colcrys® (the "Alkem ANDA Product").

54. On or about December 24, 2017, Alkem Laboratories notified Takeda of the submission of the Alkem ANDA to the FDA. As filed, the Alkem ANDA sought approval to

engage in the commercial use, manufacture, sale, offer for sale, or importation of the Alkem ANDA Product to treat FMF. (*See also* D.I. 8, C.A. No. 18-cv-189-RGA, Answer to ¶ 37) ("Alkem admits that the Alkem ANDA seeks approval from the FDA for generic colchicine tablets for the treatment of FMF.").

55. On February 1, 2018, Takeda sued Alkem in this District asserting that the filing of the Alkem ANDA was an act of infringement and that the Alkem ANDA Product, if sold and marketed, would infringe all of the Patents-in-Suit (*i.e.*, all seventeen patents listed in the Orange Book for Colcrys®).

56. During litigation, Alkem admitted to submitting a "carve-out" statement under 35 U.S.C. § 355(j)(2)(A)(viii) to the FDA with respect to the Gout Patents (except for the two overlapping FMF and Gout Patents) whereby Alkem stated that "Alkem admits that the Paragraph IV Notice Letter does not state that Alkem is seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of the Alkem ANDA Product for the treatment or prevention of gout flares" and that "Alkem admits, however, that it has submitted a statement under 21 U.S.C. § 355(j)(2)(A)(viii) to the FDA with respect to Takeda's Gout Patents." (*See* D.I. 8, C.A. No. 18-cv-189-RGA, Answer to ¶¶ 48, 77).

1. Takeda Settled Its Infringement Claims Against Alkem

57. On May 23, 2018, after an arms-length negotiation, Takeda and Alkem entered into the Settlement Agreement.

58. The Settlement Agreement provided, among other things, that Takeda would stipulate to dismiss its pending patent lawsuit without prejudice and that Alkem would, pursuant to terms set forth in the License Agreement, refrain from making, using, importing, marketing, offering for sale, selling, or distributing the Alkem ANDA Product in the United States until the earliest of a number of defined "Generic Entry Dates." (Ex. A, Settlement Agr't ¶ 3 and

License Agr't § 1.2). Beginning on the earliest of those Generic Entry Dates, Alkem would enjoy a fully paid-up, royalty-free, irrevocable, non-exclusive license under Takeda's Colcrys® patents (*i.e.*, Patents-in-Suit), to the extent necessary to manufacture, have manufactured, use, import, distribute, market, offer to sell, have sold, and sell the Alkem ANDA Product in the United States.

59. Section 1.2 of the License Agreement defines the possible Generic Entry Dates upon which Alkem may make, use, import, market, offer for sale, sell, and distribute the Alkem ANDA Product in the United States. Section 1.2(a) provides a date certain of [redacted], upon which Alkem may enter the market. (Ex. A, License Agr't § 1.2). The other possible Generic Entry Dates, set forth in Section 1.2(b) through (g) of the License Agreement, apply only when certain conditions are satisfied. (Ex. A, License Agr't § 1.2).

60. None of the Generic Entry Dates described in Section 1.2 of the License Agreement currently apply or authorize Alkem to make, use, import, market, offer for sale, sell, or distribute the Alkem ANDA Product in the United States. Therefore, pursuant to Section 1.2(a), Alkem may currently launch the Alkem ANDA Product no earlier than [redacted]. (Ex. A, License Agr't § 1.2).

61. The License Agreement establishes conditions governing "pre-booking activities" that Alkem may undertake in preparation for launching the Alkem ANDA Product. Pursuant to Section 1.4 of the License Agreement, beginning [redacted] prior to the earliest applicable Generic Entry Date, Alkem may manufacture, import, and store a reasonable inventory of the Alkem ANDA Product. (Ex. A, License Agr't § 1.4). Then, beginning [redacted] prior to the earliest applicable Generic Entry Date, Alkem may engage in discussions with potential customers to make them aware of the upcoming availability of the Alkem ANDA Product. (Ex.

A, License Agr't § 1.4). At [redacted] prior to the earliest applicable Generic Entry Date, Alkem may engage in booking sales orders for the Alkem ANDA Product. (Ex. A, License Agr't § 1.4).

62. Alkem is prohibited from selling, launching, distributing, or shipping to customers the Alkem ANDA Product before the earliest applicable Generic Entry Date. (Ex. A, License Agr't § 1.2). Because no possible Generic Entry Date other than the date certain described in Section 1.2(a) currently applies, Alkem may commence limited pre-booking activities no earlier than [redacted], as specified in Section 1.4 of the License Agreement. (Ex. A, License Agr't § 1.4).

63. In Section 1.8 of the License Agreement, Alkem acknowledged that the Patents-in-Suit are valid and enforceable, and further, Alkem acknowledged that the commercial manufacture, use, offer for sale, sale, or importation of the Alkem ANDA Product, unless licensed by Takeda, would infringe the Patents-in-Suit. (Ex. A, License Agr't § 1.8).

64. In Section 1.10 of the License Agreement, Alkem agreed that Takeda shall be entitled to immediate injunctive relief to prevent, and specific enforcement to remedy, any breach of Sections 1.2 or 1.4 of the License Agreement. (Ex. A, License Agr't § 1.10). Alkem further acknowledged that "marketing the Alkem ANDA Product in breach of Section 1.2 of the License Agreement would cause Takeda irreparable harm." (Ex. A, License Agr't § 1.10).

65. Following execution of the Settlement Agreement and License Agreement, Takeda and Alkem signed and jointly filed a stipulation voluntarily dismissing the pending litigation, attached hereto as Exhibit V. On July 6, 2018, this Court so-ordered that stipulation, and retained jurisdiction to enforce the parties' Settlement Agreement. (Ex. B, Order).

2. Takeda's Settlements with Alkem's Competitors

66. In addition to Alkem, several other generic-drug manufacturers have submitted ANDAs to the FDA seeking approval to make and sell generic versions of Colcrys®. Over several years, Takeda filed and settled litigations against each of these ANDA applicants.

67. The other ANDA applicants with whom Takeda has settled include: Par Pharmaceutical Companies, Inc. and Par Pharmaceutical, Inc. ("Par"); Watson Laboratories, Inc.; Amneal Pharmaceuticals LLC; Granules Pharmaceuticals Inc.; Mylan Pharmaceuticals, Inc.; Hetero Labs Limited, Hetero Labs Limited Unit-V, and Hetero USA Inc.; Macleods Pharma USA, Inc. and Macleods Pharmaceuticals Ltd.; Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc.; Strides Pharma Global PTE Limited and Strides Pharma Inc.; and Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Limited.

68. Generally speaking, those settlements authorize the licensed generic-drug manufacturers to begin marketing their own generic versions of Colcrys® within the United States upon a date certain or earlier if specified conditions are met.

ALKEM'S ACTIONS GIVING RISE TO THIS SUIT

A. Alkem's Breach of the License Agreement with Takeda

69. On or about February 8, 2019, the FDA approved the Alkem ANDA.

70. Upon information and belief, in or around February 2020, Alkem has begun manufacturing, having manufactured, storing, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States.

71. A generic-drug manufacturer generally must undertake substantial preparations before introducing a drug to the United States market. For example, the manufacturer must manufacture, or arrange to have manufactured, a sufficient quantity of the drug to satisfy anticipated demand upon market entry. It must store that inventory pending market entry. It

must solicit orders from wholesalers, retailers, and other customers. And it must arrange for product importation, distribution, and other logistics. Because each of these tasks is time- and resource-consuming and requires the negotiation of often complex and interlocking contracts, they typically require weeks or months to complete.

72. Upon information and belief, Alkem has made preparations for the commercial manufacture, use, offer for sale, sale, and/or importation of the Alkem ANDA Product in the United States. Specifically, upon information and belief, Alkem has begun manufacturing the Alkem ANDA Product and/or arranging for its manufacture; storing the Alkem ANDA Product; importing the Alkem ANDA Product into the United States; taking other steps to develop an inventory of the Alkem ANDA Product; discussing the Alkem ANDA Product's upcoming availability with potential customers; and recording drug pricing data of the Alkem ANDA Product on subscription-based pricing databases.

73. Upon information and belief, Ascend Laboratories has at least begun to market and/or offer to sell the Alkem ANDA Product to [redacted]. *See Wesley Jessen Corp. v. Bausch & Lomb, Inc.*, 256 F. Supp. 2d 228, 235 (D. Del. 2003) ("The Court concludes that an unauthorized offer to sell a patented product, which offer is made in the United States, is a violation of 35 U.S.C. § 271(a)").

74. Upon information and belief, in or around February 2020, Ascend Laboratories and/or Alkem Laboratories began recording pricing data for the Alkem ANDA Product in subscription-based pricing databases. (*See* Ex. W, ProspectoRx; Ex. X, Medi-Span Price Rx).

75. Upon information and belief, in or around February 2020, Alkem informed [redacted] that Alkem had a stored supply of the Alkem ANDA Product.

76. Upon information and belief, in or around March 2020, Alkem began informing the pharmaceutical industry that a launch of the Alkem ANDA Product was imminent.

77. Upon information and belief, in or around March 2020, Alkem began soliciting orders from a pharmaceutical group purchasing organization.

78. Upon information and belief, Ascend Laboratories and/or Alkem Laboratories has begun to import the Alkem ANDA Product to distribute throughout the United States. Specifically, Alkem's prescribing information and medication guide states the Alkem ANDA Product is "Manufactured in India by: Alkem Laboratories Limited" and "Distributed by: Ascend Laboratories, LLC." (*See* Ex. Y, Alkem's Label.)

79. Upon information and belief based on market intelligence, Ascend Laboratories has begun the process of notifying customers of the availability of the Alkem ANDA Product. For example, Alkem had discussions with [redacted]

80. Upon information and belief, in or around March 2020, Alkem has sold or is imminently about to sell the Alkem ANDA Product. Upon information and belief, the Alkem ANDA Product has been sold or will be sold with its label containing instructions for use by doctors, pharmacists, other healthcare professionals, and patients.

81. Alkem's preparations to launch the Alkem ANDA Product breaches the License Agreement as does any launch, offer to sell, or sale of the Alkem ANDA Product.

B. Alkem's Induced Infringement of the FMF Patents

82. Takeda's FDA approved product label for Colcrys® teaches and encourages, *inter alia*, methods of using Colcrys® claimed in the FMF Patents, including the use of colchicine to treat FMF when a patient is or is not taking another substance. (*See, e.g.*, Ex. Z, Colcyrs® Label at Table 1).

83. The approved labeling for Colcrys® directs doctors, pharmacists, other healthcare professionals, and patients to practice the claimed methods of Takeda's FMF Patents.

84. Under the Federal Food, Drug, and Cosmetic Act, drug products submitted to the FDA for approval via an ANDA are required to have the same labeling as the reference listed drug, here Colcrys®, except for changes required because of differences approved under a suitability petition (21 U.S.C. § 355(j)(2)(C); 21 C.F.R. § 314.93), because the generic drug product and reference listed drug are produced or distributed by different manufacturers (21 U.S.C. §355(j)(2)(A)(v); 21 C.F.R. §314.94(a)(8)(iv)), or because the ANDA applicant has made a section viii carve-out for one of the indications on the label of the reference listed drug.

85. Upon information and belief, the approved label for Alkem generic Colcrys® (colchicine) product (revised: 3/2018) is available online at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a4284783-fea6-4af2-9a8d-79c929176c05, a copy of which is attached hereto as Exhibit Y. Upon information and belief, Alkem's approved product is indicated for the treatment of FMF in adults and children 4 years or older.

86. Upon information and belief, the approved label for the Alkem ANDA Product directs doctors, pharmacists, other healthcare professionals, and patients to practice the following dosing information for FMF:

> The recommended dosage of colchicine tablets for FMF in adults is 1.2 mg to 2.4 mg daily.
>
> Colchicine tablets should be increased as needed to control disease and as tolerated in increments of 0.3 mg/day to a maximum recommended daily dose. If intolerable side effects develop, the dose should be decreased in increments of 0.3 mg/day. The total daily colchicine tablets dose may be administered in one to two divided doses.

(Ex. Y, Alkem's Label at § 2.2). Additionally, upon information and belief, the approved label for the Alkem ANDA Product directs doctors, pharmacists, other healthcare professionals, and patients to practice the following dosing information for pediatric patients:

> The recommended dosage of colchicine tablets for FMF in pediatric patients 4 years of age and older is based on age. The following daily doses may be given as a single or divided dose twice daily:
>
> Children 4 to 6 years: 0.3 mg to 1.8 mg daily
>
> Children 6 to 12 years: 0.9 mg to 1.8 mg daily
>
> Adolescents older than 12 years: 1.2 mg to 2.4 mg daily

(Ex. Y, Alkem's Label at § 2.3).

87. Upon information and belief, the approved label for the Alkem ANDA Product directs doctors, pharmacists, other healthcare professionals, and patients to practice the claimed methods of the FMF Patents. The Alkem ANDA Product label states that "[c]oadministration of colchicine tablets with drugs known to inhibit CYP3A4 and/or P-glycoprotein (P-gp) increases the risk of colchicine-induced toxic effects (*Table 1*). If patients are taking or have recently completed treatment with drugs listed in Table 1 within the prior 14 days, the dose adjustments are as shown on the table below *[see DRUG INTERACTIONS (7)]*." (Ex. Y, Alkem's Label at § 2.4; *see also id.* § 7 ("Table 1 provides recommendations for strong and moderate CYP3A4 inhibitors and P-gp inhibitors.")). Table 1 is reproduced *in part* below:

Strong CYP3A4 Inhibitors†			
		FMF	
Drug	**Noted or Anticipated Outcome**	**Original Intended Dosage**	**Adjusted Dose**
Atazanavir Clarithromycin Darunavir/ Ritonavir‡ Indinavir Itraconazole Ketoconazole Lopinavir/ Ritonavir‡ Nefazodone Nelfinavir Ritonavir Saquinavir Telithromycin Tipranavir/Ritonavir‡	Significant increase in colchicine plasma levels*; fatal colchicine toxicity has been reported with clarithromycin, a strong CYP3A4 inhibitor. Similarly, significant increase in colchicine plasma levels is anticipated with other strong CYP3A4 inhibitors.	Maximum daily dose of 1.2 – 2.4 mg	Maximum daily dose of 0.6 mg (may be given as 0.3 mg twice a day)
Moderate CYP3A4 Inhibitors			
		FMF	
Drug	**Noted or Anticipated Outcome**	**Original Intended Dosage**	**Adjusted Dose**
Amprenavir‡ Aprepitant Diltiazem Erythromycin Fluconazole Fosamprenavir‡ (pro-drug of Amprenavir) Grapefruit juice Verapamil	Significant increase in colchicine plasma concentration is anticipated. Neuromuscular toxicity has been reported with diltiazem and verapamil interactions.	Maximum daily dose of 1.2 – 2.4 mg	Maximum daily dose of 1.2 mg (may be given as 0.6 mg twice a day)
P-gp Inhibitors†			
		FMF	
Drug	**Noted or Anticipated Outcome**	**Original Intended Dosage**	**Adjusted Dose**
Cyclosporine Ranolazine	Significant increase in colchicine plasma levels*; fatal colchicine toxicity has been reported with cyclosporine, a P-gp inhibitor. Similarly, significant increase in colchicine plasma levels is anticipated with other P-gp inhibitors.	Maximum daily dose of 1.2 –2.4 mg	Maximum daily dose of 0.6 mg (may be given as 0.3 mg twice a day.

(Ex. Y, Alkem's Label at Table 1).

88. Upon information and belief, the approved label for the Alkem ANDA Product directs doctors, pharmacists, other healthcare professionals, and patients to practice dose adjustments for colchicine when co-administered with ketoconazole, ritonavir, clarithromycin, and other drugs. These dose adjustments are disclosed and claimed in the FMF Patents. For example, claim 1 of the '298 patent recites the following:

> 1. A method of using colchicine for the treatment of Familial Mediterranean Fever in a human adult or child > 12 years of age in need of treatment thereof, said method comprising:
>
> orally administering a reduced colchicine dosage amount to the human adult or child > 12 years of age in need of treatment for Familial Mediterranean Fever who is concomitantly receiving administration of clarithromycin within 1 to 2 days of oral administration of colchicine,
>
> wherein the reduced colchicine dosage amount is reduced compared to a daily dosage amount to be administered in the absence of concomitant clarithromycin,
>
> wherein the daily dosage amount to be administered in the absence of concomitant clarithromycin is a maximum of 2.4 mg per day, and wherein the reduced colchicine dosage amount is a maximum of 0.6 mg per day.

(Ex. E, claim 1). The dose adjustment table, Table 1 in the approved label for the Alkem ANDA Product, provides that the usual intended dose of colchicine for FMF is a maximum of 2.4 mg. (Ex. Y, Alkem's Label). When colchicine is used with a strong CYP3A4 inhibitor such as clarithromycin, the label teaches that it should be adjusted from 2.4 mg per day to a reduced colchicine dosage of 0.6 mg per day (which may be given as 0.3 mg twice per day). (Ex. Y, Alkem's Label).

89. Upon information and belief, the approved label for the Alkem ANDA Product contains a Table 6, which describes doses of co-administered, such as ketoconazole, ritonavir, clarithromycin, and others.

90. Accordingly, upon information and belief, the approved label for the Alkem ANDA Product, like the labeling for Colcrys®, recites methods of using colchicine disclosed and claimed in the FMF Patents.

91. Upon information and belief, the approved label for Alkem ANDA Product, like the labeling for Colcrys®, directs doctors, pharmacists, other healthcare professionals, and patients to practice the claimed methods of the FMF Patents. (*See, e.g.*, Ex. Y, Alkem's Label).

92. Upon information and belief, Alkem's label demonstrates Alkem's specific intent that, when concomitant administration is necessary or desirable, a doctor, pharmacist, other healthcare professional, or patient administer the Alkem ANDA Product according to the instructions on Alkem's labeling regarding dose reduction during concomitant administration, and thus directly infringe one or more claims of the FMF Patents.

93. Accordingly, upon information and belief, the Alkem ANDA Product will be administered for the treatment of FMF.

94. Upon information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and ketoconazole for a fungal infection. Upon information and belief, patients concomitantly taking ketoconazole with colchicine will be prescribed the Alkem ANDA Product according to the instructions on Alkem's labeling regarding dose reductions in accordance with the '648 Patent by doctors or other healthcare professionals. Such doctors, healthcare professionals, and patients thus will directly infringe one or more claims of the '648 Patent.

95. Upon information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and ritonavir for HIV or other viral infections. Upon information and belief, patients concomitantly taking ritonavir with colchicine will be

prescribed the Alkem ANDA Product according to the instructions on Alkem's labeling regarding dose reductions in accordance with the '519 and '297 Patents by doctors or other healthcare professionals. Such doctors, healthcare professionals, and patients thus will directly infringe one or more claims of the '519 and '297 Patents.

96. Upon information and belief, some FMF patients will undergo concomitant treatment with colchicine for FMF and clarithromycin for bacterial infections, including *H. pylori*. Upon information and belief, patients concomitantly taking clarithromycin with colchicine will be prescribed the Alkem ANDA Product according to the instructions on Alkem's labeling regarding dose reductions in accordance with the '731 and '298 Patents by doctors or other healthcare professionals. Such doctors, healthcare professionals, and patients thus will directly infringe one or more claims of the '731 and '298 Patents.

97. Upon information and belief, Alkem will induce others to infringe one or more claims of the FMF Patents. Specifically, Alkem's label explicitly instructs doctors, pharmacists, other healthcare professionals, and patients to administer the Alkem ANDA Product according to methods claimed in one or more claims of the FMF Patents. Such inducement is undertaken by Alkem with full awareness of all of the FMF Patents, each of which was asserted by Takeda in *Takeda Pharmaceuticals U.S.A., Inc. v. Alkem Laboratories Ltd. and Ascend Laboratories. LLC*, C.A. No. 18-cv-189-RGA, and identified in the Settlement Agreement and accompanying License Agreement. (*See* Ex. A, License Agr't, Definition of "Licensed Patents"). Such inducement is undertaken by Alkem, upon information and belief, with full awareness and intent that Alkem's actions and the actions of the induced persons would infringe the FMF Patents.

C. Alkem's Induced Infringement of the Gout Patents

98. Upon information and belief, Alkem has knowledge of Takeda's Gout Patents, which are listed in the Orange Book for Colcrys® and for which, upon information and belief, Alkem submitted a section viii "carve-out" statement to the FDA.

99. Upon information and belief, Alkem has made, and continues to make, substantial preparations in the United States for the commercial manufacture, use, offer for sale, sale, and/or importation of the Alkem ANDA Product prior to the expiration of the Patents-in-Suit and before the time allowed by the License Agreement.

100. Upon information and belief, Alkem intends to manufacture, offer for sale, and sell the Alkem ANDA Product in quantities that far exceed the market for treatment of FMF. Upon information and belief, Alkem knows of Takeda's Gout Patents, and knows that the Alkem ANDA Product will be sold to the gout market for the treatment and prevention of gout flares in a manner that infringes Takeda's Gout Patents.

101. Alkem received FDA approval on February 8, 2019 to sell the Alkem ANDA Product only to treat FMF. (Ex. AA, FDA's Alkem Approval). Based on the FDA-approved prescribing information, Alkem has "carved out" the gout indication from its label, thus certifying to the FDA that it will not market the Alkem ANDA Product for the treatment of gout. (Ex. Y, Alkem's Label).

102. Despite Alkem's label "carving out" the gout indication, Alkem ANDA Product will be sold in the gout market inevitably or will be used for the prophylaxis and treatment of gout flares.

103. Upon information and belief, the Alkem ANDA Product will be substantially used for the treatment and prevention of gout flares. The primary indication for Colcrys®, and the

one responsible for the vast majority of Colcrys® sales, relates to gout, which affects far more patients in the United States than does FMF.

104. Moreover, many pharmacies will fill Colcrys® or colchicine prescriptions to gout patients with the Alkem ANDA Product. In some states, such substitution will be mandatory and required by law. In others, individual pharmacists will be incentivized to substitute the Alkem ANDA Product for Colcrys® because of the lower patient cost and larger pharmacy profit margins associated with generic products.

105. Additionally, Alkem has indicated on its website at https://www.alkemlabs.com/rx-products.php (last visited Mar. 3, 2020) under RX Products that the "Therapy Area" for the Alkem ANDA Product is "Anti-Gout." (Ex. BB, Alkem RX Products).

106. Upon information and belief, Alkem also offers in its prescribing information certain instructions concerning the administration of the Alkem ANDA Product in gout patients, specifically that "[g]out is rare in pediatric patients; safety and effectiveness of colchicine in pediatric patients has not been established." (Ex. Y, Alkem's Label).

107. Upon information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and ketoconazole for a fungal infection. Upon information and belief, the Alkem ANDA Product will be sold to the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking ketoconazole. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication.

108. Upon information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and ritonavir for HIV or other viral infections. Upon information and belief, the Alkem ANDA Product will be sold to the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking ritonavir. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication.

109. Upon information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and clarithromycin for bacterial infections, including *H. pylori*. Upon information and belief, the Alkem ANDA Product will be sold to the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking clarithromycin. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication.

110. Upon information and belief, some gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and verapamil for hypertension, angina pectoris, cardiac arrhythmia, and/or other disorders. Upon information and belief, the Alkem ANDA Product will be sold to the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking verapamil. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication.

111. Upon information and belief, the Alkem ANDA Product will be sold in the gout market and will be used to treat and prevent gout flares, including in patients concomitantly taking ketoconazole, ritonavir, clarithromycin, and/or verapamil. This is because, as discussed above, physicians generally prescribe generic drugs for all of the approved indications associated with the branded drug, whether or not the generic drug is approved for that indication.

112. The expected uses of the Alkem ANDA Product in the gout market will infringe Takeda's patented low-dose method of using colchicine to treat acute gout flares or Takeda's patented methods of using colchicine to prevent or treat gout flares in patients concomitantly taking ketoconazole, ritonavir, clarithromycin, and/or verapamil, because Takeda's patented methods represent the standard of care for gout flare treatment and prevention.

* * * *

113. Upon information and belief, Alkem has engaged and will continue to engage in conduct described above that will cause third parties—such as physicians and patients—to directly infringe one or more claims of each of the Patents-in-Suit.

COUNT I

(Breach of the License Agreement)

114. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

115. Takeda and Alkem are parties to the Settlement Agreement and License Agreement, which are valid and enforceable.

116. Alkem has breached the License Agreement by marketing the Alkem ANDA Product prior to any of the Generic Entry Dates set forth in Paragraph 1.2 of the License Agreement.

117. Alkem has materially breached the License Agreement by manufacturing, having manufactured, importing, storing an amount of the Alkem ANDA Product, developing an inventory of the Alkem ANDA Product, discussing with potential customers to make them aware of the upcoming availability of the Alkem ANDA Product, marketing, recording drug pricing data of the Alkem ANDA Product on subscription-based pricing databases, and/or offering to sell the Alkem ANDA Product prior to the time set forth in Section 1.4 of the License Agreement.

118. Each unauthorized sale of the Alkem ANDA Product has proximately caused, and continues to cause, harm to Takeda by reducing the number of units and the price per unit of Colcrys® that Takeda is able to sell. In addition, Alkem's sustained launch likely will cause Takeda to incur irreversible price erosion and long-term loss of market share, both of which are irreparable injuries. Furthermore, as discussed above, other generic competitors also will be incentivized to enter the market if Alkem's at-risk launch is not enjoined. The impact to Takeda of this market competition is likely to be immediate and devastating.

119. Each unauthorized sale of the Alkem ANDA Product has proximately caused, and continues to cause, harm to Takeda by reducing the number of units and the price per unit of the authorized generic colchicine product that Par is able to sell. In addition, Alkem's sustained launch likely will cause Takeda to incur irreversible price erosion and long-term loss of market share, both of which are irreparable injuries. Furthermore, as discussed above, other generic competitors also will be incentivized to enter the market if Alkem's at-risk launch is not enjoined.

120. Absent prompt injunctive relief, Alkem's unauthorized sale of the Alkem ANDA Product inevitably will lead to irreparable harm including, but not limited to, price erosion, loss

of goodwill, reputational harm, and loss of business opportunities. Indeed, Alkem has admitted that marketing the Alkem ANDA Product in breach of Paragraph 1.2 of the License Agreement will cause Takeda irreparable harm.

121. As Alkem acknowledged in the License Agreement, Takeda is entitled to specific enforcement of the terms and conditions set forth in Sections 1.2 and 1.4 of the License Agreement, and Takeda is entitled to immediate injunctive relief to prevent Alkem from marketing the Alkem ANDA Product in breach of Sections 1.2 and 1.4 of the License Agreement. (Ex. A, License Agr't § 1.10).

COUNT II

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '519 Patent)

122. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

123. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '519 patent.

124. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '519 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '519 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

125. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '519 patent.

COUNT III

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '731 Patent)

126. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

127. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '731 patent.

128. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '731 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '731 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

129. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '731 patent.

COUNT IV

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '298 Patent)

130. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

131. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '298 patent.

132. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '298 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '298 patent under 35 U.S.C. § 271(b) by causing direct infringement as

133. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '298 patent.

COUNT V

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '648 Patent)

134. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

135. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '648 patent.

136. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '648 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '648 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

137. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '648 patent.

COUNT VI

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '297 Patent)

138. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

139. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '297 patent.

140. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '297 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '297 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

141. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '297 patent.

COUNT VII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '004 Patent)

142. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

143. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '004 patent.

144. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '004 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '004 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

145. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '004 patent.

COUNT VIII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '758 Patent)

146. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

147. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '758 patent.

148. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '758 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '758 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

149. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '758 patent.

COUNT IX

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '681 Patent)

150. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

151. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '681 patent.

152. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '681 patent and without license or authorization from Takeda, Alkem will induce infringement of one

or more claims of the ’681 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

153. Alkem’s imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the ’681 patent.

COUNT X

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the ’269 Patent)

154. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

155. In Section 1.8(b) of the License Agreement, Alkem agreed “not to challenge to the infringement, validity, and enforceability” of the ’269 patent.

156. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the ’269 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the ’269 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

157. Alkem’s imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the ’269 patent.

COUNT XI

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the ’647 Patent)

158. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

159. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '647 patent.

160. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '647 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '647 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

161. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '647 patent.

COUNT XII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '938 Patent)

162. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

163. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '938 patent.

164. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '938 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '938 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

165. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '938 patent.

COUNT XIII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '296 Patent)

166. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

167. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '296 patent.

168. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '296 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '296 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

169. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '296 patent.

COUNT XIV

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '655 Patent)

170. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

171. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '655 patent.

172. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '655 patent and without license or authorization from Takeda, Alkem will induce infringement of one

or more claims of the ’655 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

173. Alkem’s imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the ’655 patent.

COUNT XV

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the ’395 Patent)

174. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

175. In Section 1.8(b) of the License Agreement, Alkem agreed “not to challenge to the infringement, validity, and enforceability” of the ’395 patent.

176. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the ’395 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the ’395 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

177. Alkem’s imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the ’395 patent.

COUNT XVI

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the ’396 Patent)

178. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

179. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '396 patent.

180. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '396 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '396 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

181. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '396 patent.

COUNT XVII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '721 Patent)

182. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

183. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '721 patent.

184. By manufacturing, having manufactured, importing, marketing, offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '721 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '721 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

185. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '721 patent.

COUNT XVIII

(Declaratory Judgment of Infringement Under 35 U.S.C. § 271(b) of the '722 Patent)

186. Takeda restates and incorporates by reference its previous allegations above, as if fully set forth herein.

187. In Section 1.8(b) of the License Agreement, Alkem agreed "not to challenge to the infringement, validity, and enforceability" of the '722 patent.

188. By manufacturing, having manufactured, importing, marketing, , offering to sell, and/or selling the Alkem ANDA Product in the United States prior to the expiration of the '722 patent and without license or authorization from Takeda, Alkem will induce infringement of one or more claims of the '722 patent under 35 U.S.C. § 271(b) by causing direct infringement as described above, such as in ¶ 110.

189. Alkem's imminent infringing activities will cause Takeda to suffer irreparable harm unless and until this Court issues a declaratory judgment of infringement of the '722 patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully requests the following relief:

A. A judgment and declaration that Alkem has breached the express terms of the License Agreement;

B. An order directing Alkem to specifically perform its obligations under the License Agreement;

C. A declaratory judgment of infringement of the Patents-in-Suit, under 35 U.S.C. § 271(b) and 28 U.S.C. §§ 2201 and 2202;

D. An entry of injunctive relief enjoining and restraining Alkem and its affiliates, subsidiaries, directors, employees, agents, representatives, licensees, successors, assigns, and all

other persons acting or attempting to act in active concert or participation with it or acting on its behalf, from further infringement of the Patents-in-Suit, or from further breaching any contractual obligation owed by Alkem to Takeda;

E. A judgment awarding Takeda all damages resulting from Alkem's breaches of the License Agreement in an amount in excess of $75,000;

F. An order declaring this an exceptional case under 35 U.S.C. § 285 and awarding Takeda its reasonable attorneys' fees, costs, and expenses;

G. An order requiring Alkem to recall, remove, or destroy all the Alkem ANDA Product that has been introduced to the market;

H. An award of pre- and post-judgment interest, and the taxation of all allowable costs against Alkem; and

I. For such other and further relief as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Takeda demands a jury trial on all issues that are triable to a jury.

Dated: March 3, 2020

/s/ Francis DiGiovanni
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