IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

THERAVANCE BIOPHARMA R&D IP, LLC, THERAVANCE BIOPHARMA US, INC., THERAVANCE BIOPHARMA IRELAND LIMITED, MYLAN IRELAND LIMITED, and MYLAN SPECIALTY L.P.,	)	
Plaintiffs,	)	C.A. No.
v.	)	
LUPIN INC., LUPIN LTD., and LUPIN PHARMACEUTICALS, INC.,	)	
Defendants.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Theravance Biopharma R&D IP, LLC, Theravance Biopharma Ireland Limited, Theravance Biopharma US, Inc., Mylan Ireland Limited, and Mylan Specialty L.P. (collectively, "Plaintiffs"), by their attorneys, for their Complaint against Defendants Lupin Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc. ("Lupin Pharmaceuticals") (collectively, "Lupin" or "Defendants"), hereby allege as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 8,541,451 (the "'451 patent"), 9,765,028 (the "'028 patent"), 10,550,081 (the "'081 patent"), 11,008,289 (the "'289 patent"), and 11,484,531 (the "'531 patent") (collectively, the "Patents-in-Suit") arising under the Patent Laws of the United States, Title 35, United States Code, Section 1 *et seq*. This action relates to Abbreviated New Drug Application ("ANDA") No. 218088, filed by Lupin, with the United States Food and Drug Administration ("FDA") for approval to market a generic version of YUPELRI® (revefenacin) inhalation solution, for oral inhalation, prior to the expiration of

patents listed in FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book") for YUPELRI®.

THE PARTIES

Plaintiffs

2. Plaintiff Theravance Biopharma R&D IP, LLC is a Delaware limited liability company having a principal place of business at 901 Gateway Boulevard, South San Francisco, CA, 94080.

3. Plaintiff Theravance Biopharma US, Inc. is a Delaware corporation having a principal place of business at 901 Gateway Boulevard, South San Francisco, CA, 94080.

4. Plaintiff Theravance Biopharma Ireland Limited is an Irish company having a registered office at Ten Earlsfort Terrace, Dublin 2, D02 T380, Ireland.

5. Plaintiff Mylan Ireland Limited is a company having a principal place of business at Newenham Court, Northern Cross, Malahide Road, Dublin 17, Ireland; and a registered office at Unit 35/36, Grange Parade, Baldoyle Industrial Estate, Dublin 13, Ireland.

6. Plaintiff Mylan Specialty L.P. is a company having a principal place of business at 3711 Collins Ferry Road, Morgantown, West Virginia, 26505.

7. Plaintiff Mylan Specialty L.P. sells YUPELRI® in this judicial district and throughout the United States.

8. Plaintiffs Mylan Specialty L.P. and Theravance Biopharma US, Inc. promote and market YUPELRI® in the United States.

9. Theravance Biopharma R&D IP, LLC is the assignee of the Patents-in-Suit. Theravance Biopharma R&D IP, LLC is a wholly owned subsidiary of Theravance Biopharma Ireland Limited.

10. Theravance Biopharma Ireland Limited is the exclusive licensee, and Mylan Ireland Limited is the exclusive sub-licensee, of the Patents-in-Suit. Mylan Ireland Limited is also the

holder of approved New Drug Application No. 210598 for YUPELRI® (revefenacin) inhalation solution, for oral inhalation (the "YUPELRI® NDA").

Lupin

11. On information and belief, Defendant Lupin Inc. is a company organized and existing under the laws of the State of Delaware, with its principal place of business at 111 South Calvert Street, Harborplace Tower, 21st Floor, Baltimore, Maryland 21202.

12. On information and belief, Defendant Lupin Ltd. is a company organized and existing under the laws of India, with its principal place of business at B/4 Laxmi Towers, Bandra Kurla Complex Bandra (E), Mumbai, 400051, India.

13. On information and belief, Defendant Lupin Pharmaceuticals is a company organized and existing under the laws of Delaware, with it principal place of business at 111 South Calvert Street, Harborplace Tower, 21st Floor, Baltimore, Maryland 21202.

14. On information and belief, Lupin Inc. is a wholly owned subsidiary of Lupin Ltd.

15. On information and belief, Lupin Pharmaceuticals is a wholly owned subsidiary of Lupin Ltd.

16. On information and belief, Lupin Inc., Lupin Ltd., and Lupin Pharmaceuticals acted in concert to prepare and submit ANDA No. 218088 (the "Lupin ANDA") to FDA to engage in the commercial manufacture, use, sale or offer for sale within or importation into, the United States, including, on information and belief, in the State of Delaware, of a generic version of YUPELRI® (revefenacin) inhalation solution (the "Lupin ANDA Product"), for oral inhalation, prior to the expiration of the Patents-in-Suit.

17. On information and belief, following any FDA approval of the Lupin ANDA, Lupin Inc., Lupin Ltd., and Lupin Pharmaceuticals will act in concert to commercially manufacture, import, market, offer for sale, distribute, and/or sell the Lupin ANDA Product throughout the United States, including within the State of Delaware.

JURISDICTION AND VENUE

18. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

19. This action arises under the patent laws of the United States, 35 U.S.C. § 1, *et seq*., including 35 U.S.C. § 271.

20. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a), and 28 U.S.C. §§ 2201 and 2202.

21. This Court has personal jurisdiction over Lupin Inc. at least because, *inter alia*, on information and belief, Lupin Inc. is a corporation organized and existing under the laws of the State of Delaware.

22. This Court has personal jurisdiction over Lupin Pharmaceuticals at least because, *inter alia*, on information and belief, Lupin Pharmaceuticals is a corporation organized and existing under the laws of the State of Delaware.

23. This Court has personal jurisdiction over Lupin Inc. at least because, on information and belief, Lupin Inc. directly or indirectly develops, manufacturers, markets and/or sells or intends to market and sell generic drugs throughout the United States and in this judicial district.

24. This Court has personal jurisdiction over Lupin Ltd. at least because, on information and belief, Lupin Ltd. directly or indirectly develops, manufacturers, markets and/or sells or intends to market and sell generic drugs throughout the United States and in this judicial district.

25. This Court has personal jurisdiction over Lupin Pharmaceuticals at least because, on information and belief, Lupin Pharmaceuticals directly or indirectly develops, manufacturers, markets and/or sells or intends to market and sell generic drugs throughout the United States and in this judicial district.

26. This Court has personal jurisdiction over Lupin Inc., Lupin Ltd., and Lupin Pharmaceuticals at least because, *inter alia*, on information and belief, (1) Lupin Inc. itself, and/or in concert with Lupin Ltd. and/or Lupin Pharmaceuticals, has filed an ANDA for the purpose of seeking approval to engage in commercial manufacture, use, offer for sale, sale, and/or importation of the Lupin ANDA Product in the United States, including the State of Delaware; and (2) Lupin Inc. itself, and/or in concert with Lupin Ltd. and/or Lupin Pharmaceuticals, will market, distribute, offer for sale, and/or sell the Lupin ANDA Product in the United States, including the State of Delaware, upon approval of ANDA No. 218088, and Lupin will derive substantial revenue from the use or consumption of the Lupin ANDA Product in the State of Delaware.

27. Upon information and belief, Lupin Inc., Lupin Ltd., and Lupin Pharmaceuticals have thus been, and continue to be, joint and prime actors in the drafting, submission, approval and maintenance of ANDA No. 218088.

28. If Lupin Ltd.'s connections with the State of Delaware are found to be insufficient to confer personal jurisdiction, then, on information and belief, Lupin Ltd. is not subject to jurisdiction in any state's courts of general jurisdiction, and exercising jurisdiction over Lupin Ltd. in the State of Delaware is consistent with the United States Constitution and laws. *See* Fed. R. Civ. P. 4(k)(2).

29. Venue is proper in this district for Lupin Ltd. pursuant to 28 U.S.C. §§ 1391 and 1400(b) at least because, *inter alia*, on information and belief, Lupin Ltd. is a foreign corporation organized and existing under the laws of India and may be sued in any judicial district in which it is subject to personal jurisdiction, including in this judicial district.

30. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400(b) as to Lupin Inc. at least because, on information and belief, Lupin Inc. is incorporated in the State of Delaware.

31. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400(b) as to Lupin Pharmaceuticals at least because, on information and belief, Lupin Pharmaceuticals is incorporated in the State of Delaware.

32. On information and belief, Lupin Inc., Lupin Ltd., and/or Lupin Pharmaceuticals have litigated previous Hatch-Waxman patent infringement disputes in the District of Delaware, including affirmatively availing itself of the jurisdiction of this Court by filing counterclaims, and have not contested jurisdiction and venue in the District of Delaware in one or more prior cases arising out of the filing of ANDAs. *See*, *e.g.*, *Neurocrine Biosciences, Inc. v. Lupin Ltd. et al.*, C.A. No. 22-cv-1061-MN (Lupin Inc., Lupin Ltd., and Lupin Pharmaceuticals); *Boehringer Ingelheim Pharms., Inc. v. Lupin Ltd. et al.*, C.A. No. 21-cv-1486-CFC (Lupin Ltd. and Lupin Pharmaceuticals); *Genentech, Inc. v. Lupin Ltd. et al.*, C.A. No. 19-cv-109-RGA (Lupin Ltd. and Lupin Pharmaceuticals); *Bayer Intell. Prop. GmbH v. Lupin Ltd.*, C.A. No. 17-cv-1047-RGA (Lupin Ltd. and Lupin Pharmaceuticals).

THE PATENTS-IN-SUIT

The ’451 Patent

33. The ’451 patent, titled “Crystalline Freebase Forms of a Biphenyl Compound,” was duly and legally issued by the United States Patent and Trademark Office (“USPTO”) on September 24, 2013. A true and correct copy of the ’451 patent is attached as Exhibit A.

34. Theravance Biopharma R&D IP, LLC is the assignee of the ’451 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the ’451 patent. Mylan Ireland Limited is the exclusive sub-licensee of the ’451 patent from Theravance Biopharma Ireland Limited.

35. The ’451 patent is listed in the Orange Book as covering YUPELRI®.

The '028 Patent

36. The '028 patent, titled "Crystalline Freebase Forms of a Biphenyl Compound," was duly and legally issued by the USPTO on September 19, 2017. A true and correct copy of the '028 patent is attached as Exhibit B.

37. Theravance Biopharma R&D IP, LLC is the assignee of the '028 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '028 patent. Mylan Ireland Limited is the exclusive sub-licensee of the '028 patent from Theravance Biopharma Ireland Limited.

38. The '028 patent is listed in the Orange Book as covering YUPELRI®.

The '081 Patent

39. The '081 patent, titled "Crystalline Freebase Forms of a Biphenyl Compound," was duly and legally issued by the USPTO on February 4, 2020. A true and correct copy of the '081 patent is attached as Exhibit C.

40. Theravance Biopharma R&D IP, LLC is the assignee of the '081 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '081 patent. Mylan Ireland Limited is the exclusive sub-licensee of the '081 patent from Theravance Biopharma Ireland Limited.

41. The '081 patent is listed in the Orange Book as covering YUPELRI®.

The '289 Patent

42. The '289 patent, titled "Crystalline Freebase Forms of a Biphenyl Compound," was duly and legally issued by the USPTO on May 18, 2021. A true and correct copy of the '289 patent is attached as Exhibit D.

43. Theravance Biopharma R&D IP, LLC is the assignee of the '289 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '289 patent. Mylan Ireland

Limited is the exclusive sub-licensee of the '289 patent from Theravance Biopharma Ireland Limited.

44. The '289 patent is listed in the Orange Book as covering YUPELRI® and its approved uses.

The '531 Patent

45. The '531 patent titled "Methods for Treating Chronic Obstructive Pulmonary Disease," was duly and legally issued by the USPTO on November 1, 2022. A true and correct copy of the '531 patent is attached as Exhibit E.

46. Theravance Biopharma R&D IP, LLC is the assignee of the '531 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '531 patent. Mylan Ireland Limited is the exclusive sub-licensee of the '531 patent from Theravance Biopharma Ireland Limited.

47. The '531 patent is listed in the Orange Book as covering YUPELRI® and its approved uses.

YUPELRI®

48. Plaintiffs are engaged in the business of creating, developing, and bringing to market innovative pharmaceutical products for the treatment of diseases.

49. Plaintiffs' YUPELRI® (revefenacin) is a prescription medicine indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease ("COPD"), a chronic inflammatory lung disease characterized by progressive persistent airflow obstruction. Revefenacin is a long-acting muscarinic antagonist, which is often referred to as an anticholinergic. It is administered long-term as one vial of YUPELRI®, one time each day, by the orally inhaled route via a jet nebulizer.

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

healthcare providers to safely and effectively administer the drug. *See* 21 C.F.R. § 201.56(a)(1)-(3), (d)(1); 21 C.F.R. § 201.57(a)-(c).

51. Consistent with FDA regulations, the package insert for YUPELRI® includes prescribing information that recites the FDA-approved indication for YUPELRI® and provides instructions for healthcare providers and patients to safely and effectively administer YUPELRI®.

52. Attached as Exhibit F is a true and correct copy of the May 2022 YUPELRI® package insert, which is the current version of the YUPELRI® package insert.

53. YUPELRI® is indicated for the maintenance treatment of patients with COPD. (Ex. F at § 1).

54. YUPELRI® was studied in two 12-week replicate placebo-controlled trials in patients with moderate to very severe COPD. The population had COPD with a mean post-bronchodilator forced expiratory volume in one second (FEV_1) percent predicted of 55% (range: 10% to 90%). (Ex. F at § 14.2).

COPD

55. COPD is a chronic inflammatory lung disease characterized by progressive persistent airflow obstruction. Bronchodilators, such as muscarinic receptor antagonists and β-adrenergic agonists, are used to treat COPD. Such bronchodilators are typically delivered to a patient in need of treatment using an inhalation delivery device, such as a dry powder inhaler, a metered dose inhaler or a nebulizer.

56. Healthcare providers use guidelines from the Global Initiative for Chronic Obstructive Lung Disease, commonly known as the GOLD guidelines, to determine treatment algorithms for COPD patients. The GOLD guidelines are regularly updated, most recently for 2023.

57. The GOLD guidelines grade COPD into mild, moderate, severe, and very severe classifications based on the severity of airflow obstruction. Airflow obstruction is measured as forced expiratory volume in one second (FEV_1). According to the GOLD guidelines, severe includes patients with a percent predicted FEV_1 of equal to or greater than 30% and less than 50%. According to the GOLD guidelines, very severe includes patients with a percent predicted FEV_1 of less than 30%.

58. The GOLD guidelines also call for healthcare providers to assess patients' ability to use an inhaler regularly. Inspiratory flow is recognized as an important factor in successfully using inhalers. The GOLD guidelines state that each dry powder inhaler has a unique internal resistance and patients must create turbulent energy within the device during inhalation to disaggregate the powder into fine particles. The GOLD guidelines continue by instructing healthcare providers to check visually that the patient can inhale forcefully through the device.

59. For many patients, any type of inhalation delivery device can be used to deliver an adequate dose of a bronchodilator. However, for COPD patients having a lower than normal inspiratory flow rate, nebulizers are sometimes recommended since these patients may be unable to generate a peak inspiratory flow rate ("PIFR") sufficient for proper use of a dry powder inhaler. *See, e.g.*, Mahler, D.A., *Peak Inspiratory Flow Rate as a Criterion for Dry Powder Inhaler Use in Chronic Obstructive Pulmonary Disease*, 14(7) Ann. Am. Thorac. Soc. 1103-07 (Jul. 2017) ("Mahler 2017"); Mahler, D.A. et al., *Comparison of dry powder versus nebulized beta-agonist in patients with COPD who have suboptimal peak inspiratory flow rate*, 27(2) J. Aerosol Med. Pulm. Drug Deliv. 103-09 (Apr. 2014) ("Mahler 2014"). Accordingly, use of a nebulizer for delivery of a bronchodilator has been suggested for COPD patients having a low PIFR.

60. Low PIFR is also referred to as suboptimal PIFR. Low or suboptimal PIFR can be readily established, for example, using the IN-CHECK DIAL® device which can, for example, simulate the resistance of a dry powder inhaler such as the DISKUS® device.

61. If the PIFR value is less than about 60 L/min, the patient may not achieve optimal clinical benefit from a dry powder inhaler. A PIFR of less than 30 L/min is insufficient for a dry powder inhaler.

ACTS GIVING RISE TO THIS ACTION

62. In a letter dated January 5, 2023, purporting to be notice under 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 (the "Lupin Notice Letter"), Lupin notified Mylan Ireland Limited and Theravance Biopharma R&D IP LLC that it had submitted ANDA No. 218088 to the FDA under Section 21 U.S.C. §§ 355(j)(1) and 2(A), seeking approval to engage in the commercial manufacture, use, or sale of its proposed revefenacin inhalation solution, for oral inhalation (the "Lupin ANDA Product"), as a generic version of YUPELRI® in/into the United States, prior to the expiration of the '451 patent, the '028 patent, the '081 patent, the '289 patent, and the '531 patent.

63. On information and belief, Lupin included in the Lupin ANDA a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Lupin Paragraph IV Certification") that, in its opinion and to the best of its knowledge, the '451 patent, the '028 patent, the '081 patent, the '289 patent, and the '531 patent are invalid, unenforceable, and/or will not be infringed by the Lupin ANDA Product.

64. Lupin filed the Lupin Paragraph IV Certification without adequate justification for asserting that the Patents-in-Suit are invalid, unenforceable, and/or not infringed by the commercial manufacture, use, offer for sale, sale, or importation in or into the United States of the Lupin ANDA Product.

65. In the Notice Letter, Lupin offered confidential access to portions of its ANDA No. 218088, on terms and conditions set forth in the Lupin Notice Letter ("the Lupin Offer"). Lupin

requested that Plaintiffs accept the Lupin Offer before receiving access to the Lupin ANDA. The Lupin Offer contained restrictions that contravene 21 U.S.C. § 355(j)(5)(C)(i)(III).

66. On information and belief, the active ingredient of the Lupin ANDA Product is revefenacin, which is the same active ingredient in YUPELRI® and the same active ingredient used in the compositions, methods of use, and processes described and claimed in one or more claims of the Patents-in-Suit.

67. On information and belief, Lupin asserts in ANDA No. 218088 that the Lupin ANDA Product is bioequivalent to YUPELRI®, refers to and relies upon the YUPELRI® NDA, and contains data that, according to Lupin, demonstrate the bioequivalence of the Lupin ANDA Product to YUPELRI®.

68. On information and belief, Lupin is seeking approval to market the Lupin ANDA Product for the same approved indication as YUPELRI®.

69. On information and belief, Lupin is seeking approval to market the Lupin ANDA Product for maintenance treatment of patients with COPD.

70. On information and belief, Lupin had knowledge of the ’451 patent, the ’028 patent, the ’081 patent, the ’289 patent, and the ’531 patent when it submitted and filed ANDA No. 218088.

71. On information and belief, Lupin intends to and will infringe, actively induce infringement, and/or contribute to infringement of one or more claims of the Patents-in-Suit upon receiving FDA approval of ANDA No. 218088 and prior to the expiration of the Patents-in-Suit.

72. On information and belief, Lupin will commercially manufacture, use, offer for sale, and/or sell the Lupin ANDA Product throughout the United States, import the Lupin ANDA Product into the United States, and/or induce and/or contribute to such acts promptly upon receiving FDA approval to do so and during the term of the Patents-in-Suit.

73. On information and belief, Lupin knows that the Lupin ANDA Product is especially made or adapted for use in a way that would infringe the Patents-in-Suit, and is not suitable for substantial non-infringing use. On information and belief, Lupin knowingly has taken and intends to take active steps to, and will, induce and/or contribute to infringement of one or more claims of the Patents-in-Suit.

74. On information and belief, Lupin uses processes covered by one or more claims of the Patents-in-Suit to prepare the Lupin ANDA Product.

75. On information and belief, the Lupin ANDA Product resulting from the processes claimed in one or more Patents-in-Suit is and/or is intended to be made, used, offered for sale, and/or sold without material change to the product resulting from the processes claimed by one or more Patents-in-Suit.

76. The Lupin ANDA Product resulting from the processes claimed by one or more Patents-in-Suit is not a nonessential and/or trivial component of another product.

77. A definite and concrete, real and substantial, justiciable, and continuing case or controversy exists between Plaintiffs and Lupin with respect to infringement of the Patents-in-Suit.

78. This action is being commenced within 45 days of receipt of the Lupin Notice Letter.

COUNT I
INFRINGEMENT OF U.S. PATENT NO. 8,541,451

79. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

80. Lupin's submission of ANDA No. 218088 containing a Paragraph IV Certification to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Lupin ANDA Product in/into the United States prior to the expiration

of the '451 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '451 patent under 35 U.S.C. § 271(e)(2)(A).

81. Lupin's commercial manufacture, sale, offer for sale, or use of the Lupin ANDA Product within the United States, or importation of the Lupin ANDA Product into the United States, during the term of the '451 patent would infringe one or more claims of the '451 patent under 35 U.S.C. § 271(a), either literally or under the doctrine of equivalents.

82. Lupin's commercial manufacture, sale, offer for sale, or use of the Lupin ANDA Product within the United States, or importation of the Lupin ANDA Product into the United States, during the term of the '451 patent would infringe one or more claims of the '451 patent under 35 U.S.C. § 271(g).

83. On information and belief, Lupin intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Lupin ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 218088 and any amendments thereto, *i.e.*, prior to the expiration of the '451 patent.

84. On information and belief, Lupin had knowledge of the '451 patent when it submitted ANDA No. 218088. Lupin's infringement has been, and continues to be, deliberate.

85. Plaintiffs will be substantially and irreparably harmed if Lupin's infringement of the '451 patent is not enjoined.

86. Plaintiffs do not have an adequate remedy at law.

COUNT II
INFRINGEMENT OF U.S. PATENT NO. 9,765,028

87. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

88. Lupin's submission of ANDA No. 218088 containing a Paragraph IV Certification to obtain approval from the FDA to engage in the commercial manufacture, importation, use,

offer for sale, and/or sale of the Lupin ANDA Product in/into the United States prior to the expiration of the '028 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '028 patent under 35 U.S.C. § 271(e)(2)(A).

89. Lupin's commercial manufacture, sale, offer for sale, or use of the Lupin ANDA Product within the United States, or importation of the Lupin ANDA Product into the United States, during the term of the '028 patent would infringe one or more claims of the '028 patent under 35 U.S.C. § 271(a), either literally or under the doctrine of equivalents.

90. On information and belief, Lupin intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Lupin ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 218088 and any amendments thereto, *i.e.*, prior to the expiration of the '028 patent.

91. On information and belief, Lupin had knowledge of the '028 patent when it submitted ANDA No. 218088. Lupin Inc.'s infringement has been, and continues to be, deliberate.

92. Plaintiffs will be substantially and irreparably harmed if Lupin's infringement of the '028 patent is not enjoined.

93. Plaintiffs do not have an adequate remedy at law.

COUNT III
INFRINGEMENT OF U.S. PATENT NO. 10,550,081

94. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

95. Lupin's submission of ANDA No. 218088 containing a Paragraph IV Certification to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Lupin ANDA Product in/into the United States prior to the

expiration of the '081 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '081 patent under 35 U.S.C. § 271(e)(2)(A).

96. Lupin's commercial manufacture, sale, offer for sale, or use of the Lupin ANDA Product within the United States, or importation of the Lupin ANDA Product into the United States, during the term of the '081 patent would infringe one or more claims of the '081 patent under 35 U.S.C. § 271(a), either literally or under the doctrine of equivalents.

97. On information and belief, Lupin intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Lupin ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 218088 and any amendments thereto, *i.e.*, prior to the expiration of the '081 patent.

98. On information and belief, Lupin had knowledge of the '081 patent when it submitted ANDA No. 218088. Lupin's infringement has been, and continues to be, deliberate.

99. Plaintiffs will be substantially and irreparably harmed if Lupin's infringement of the '081 patent is not enjoined.

100. Plaintiffs do not have an adequate remedy at law.

COUNT IV
INFRINGEMENT OF U.S. PATENT NO. 11,008,289

101. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

102. Lupin's submission of ANDA No. 218088 containing a Paragraph IV Certification to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Lupin ANDA Product in/into the United States prior to the expiration of the '289 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '289 patent under 35 U.S.C. § 271(e)(2)(A).

103. Lupin's commercial manufacture, sale, offer for sale, or use of the Lupin ANDA Product within the United States, or importation of the Lupin ANDA Product into the United States, during the term of the '289 patent would induce infringement and/or infringe one or more claims of the '289 patent under 35 U.S.C. §§ 271(b) and/or (g).

104. On information and belief, Lupin intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Lupin ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 218088 and any amendments thereto, *i.e.*, prior to the expiration of the '289 patent.

105. On information and belief, Lupin had knowledge of the '289 patent when it submitted ANDA No. 218088. Lupin's infringement has been, and continues to be, deliberate.

106. Plaintiffs will be substantially and irreparably harmed if Lupin's infringement of the '289 patent is not enjoined.

107. Plaintiffs do not have an adequate remedy at law.

COUNT V
INFRINGEMENT OF U.S. PATENT NO. 11,484,531

108. Plaintiffs incorporate by reference the prior paragraphs of this Complaint as if fully set forth herein.

109. Lupin's submission of ANDA No. 218088 containing a Paragraph IV Certification to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Lupin ANDA Product in/into the United States prior to the expiration of the '531 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '531 patent under 35 U.S.C. § 271(e)(2)(A).

110. Unless enjoined, upon FDA approval of Lupin's ANDA No. 218088, Lupin will infringe one or more claims of the '531 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

111. On information and belief, upon FDA approval of Lupin's ANDA No. 218088, Lupin intends to manufacture, market, sell, and offer to sell Lupin's ANDA Product with an FDA-approved package insert that will direct healthcare providers and patients in the use of Lupin's ANDA Product.

112. On information and belief, Lupin will actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Lupin knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '531 patent by marketing Lupin's ANDA Product with the FDA-approved package insert.

113. The '531 patent has one independent claim, claim 1, which states:

> 1. A method for treating chronic obstructive pulmonary disease in a patient, the method comprising:
>
> (a) selecting a patient having chronic obstructive pulmonary disease for treatment based on the patient having a peak inspiratory flow rate less than about 60 L/min and a percent predicted force expiratory volume in one second less than about 50 percent; and
>
> (b) administering a pharmaceutical composition comprising about 175 μg of revefenacin, or a pharmaceutically acceptable salt thereof, in 3 mL of an aqueous solution to the selected patient once daily using a nebulizer.

114. A healthcare provider will directly infringe one of more of the claims of the '531 patent. Specifically, a healthcare provider administering Lupin's ANDA Product in accordance with Lupin's package insert will perform all of the steps of one or more claims of the '531 patent.

115. FDA regulations require that approved drug products include prescribing information reciting the FDA-approved indication(s) for the drug and related instructions for healthcare providers to safely and effectively administer the drug. *See* 21 C.F.R. § 201.56(a)(1)-(3), (d)(1); 21 C.F.R. § 201.57(a)-(c).

116. Consistent with FDA regulations, the package insert for YUPELRI® includes prescribing information that recites the FDA-approved indication for YUPELRI® and provides instructions for healthcare providers and patients to safely and effectively administer YUPELRI®.

117. The package insert for Lupin's ANDA Product will be substantially similar to the package insert for YUPELRI® in all material respects.

118. Providers of revefenacin review and follow the package inserts for the revefenacin products they use to treat their patients.

119. On information and belief, Lupin is seeking approval to market its ANDA Product for the same approved indication as YUPELRI®.

120. The YUPELRI® package insert instructs that YUPELRI® is "indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD)." (Ex. F at § 1).

121. The "Dosage and Administration" section of the YUPELRI® package instructs that the "recommended dosage is 175 mcg YUPELRI (one 175 mcg unit-dose vial) administered by oral inhalation once daily by nebulizer using a mouthpiece." (Ex. F at § 2).

122. The "Dosage Form and Strengths" section of the YUPELRI® package insert states that YUPELRI® is an "Inhalation solution: 175 mcg of revefenacin in 3 mL of sterile, clear, colorless, aqueous solution in unit dose vials." (Ex. F at § 3).

123. A healthcare provider will select a patient having COPD for treatment with YUPELRI® based on the patient having a PIFR of less than about 60 L/min and a percent predicted force expiratory volume in one second less than about 50%.

124. The YUPELRI® package insert describes the treatment of moderate to very severe patients in Clinical Studies. (Ex. F at § 14.2).

125. According to the YUPELRI® package insert, in Section 14.2, the clinical trials enrolled patients with mean percent predicted FEV_1 of 55%. (*Id.*)

126. The GOLD guidelines, Table 2.6, categorize severe COPD based on FEV_1 of equal to or greater than 30% and less than 50%.

127. A healthcare provider, or a patient at the direction of a healthcare provider, will administer Lupin's ANDA Product to the patient once daily using a nebulizer.

128. The YUPELRI® package insert, in Section 2, Dosing and Administration, instructs treating patients by administering YUPELRI® by nebulizer.

129. The GOLD guidelines, such as at pages 69-70, advise healthcare providers to check the patient's ability to use an inhaler.

130. It is known that successful use of dry powder inhalers such as the HandiHaler® requires a PIFR of 60 L/min.

131. A healthcare provider will select a nebulizer for patients with a PIFR of less than about 60 L/min. *See, e.g.*, Mahler 2017; Mahler 2014.

132. On information and belief, Lupin specifically intends that its ANDA product, if marketed, would be administered to some patients with moderate to severe COPD having a PIFR of less than about 60 L/min and FEV_1 of less than 50%, using a nebulizer.

133. On information and belief, Lupin knows that some healthcare providers will select patients for treatment with YUPELRI® based on the patient having a PIFR of less than about 60 L/min and FEV_1 of less than 50%.

134. On information and belief, Lupin knows, and specifically intends, that some healthcare providers will select patients for treatment with its proposed ANDA product, if marketed, based on the patient having a PIFR of less than about 60 L/min and FEV_1 of less than 50%.

135. Plaintiffs will be substantially and irreparably harmed if Lupin's infringement of the '531 patent is not enjoined.

136. Plaintiffs do not have an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

(a) A judgment that Lupin under 35 U.S.C. § 271(e)(2)(A) has infringed one or more claims of each of the Patents-in-Suit by the filing of ANDA No. 218088;

(b) A judgment that Lupin's manufacturing, using, selling, offering for sale, and/or importing the Lupin ANDA Product in/into the United States will infringe one or more claims of each of the Patents-in-Suit under 35 U.S.C. § 271(a), (b), and/or (g);

(c) A declaration under 28 U.S.C. §§ 2201-02 that if Lupin, its officers, agents, employees, parents, affiliates, and subsidiaries, and all persons and entities acting in concert with it or on its behalf, engage in the commercial manufacture, use, offer for sale, sale or importation of the Lupin ANDA Product, it will constitute an act of infringement pursuant to 35 U.S.C. § 271(a), (b), and/or (g);

(d) A judgment under 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval of ANDA No. 218088 under Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)) be a date not earlier than the latest expiration date of the '451 patent, the '028 patent, the '081 patent, the '289 patent, and the '531 patent, inclusive of any extension(s) or additional period(s) of exclusivity;

(e) A judgment under 35 U.S.C. §§ 271(e)(4)(B) and 283 providing injunctive relief against Lupin, whether alone or in concert with a subsidiary company, to prevent the commercial manufacture, use, offer to sell, or sale within the United States, or importation into the United States of the Lupin ANDA Product before the expiration of the Patents-in-Suit, inclusive of any extension(s) to patent term;

(f) A permanent injunction restraining and enjoining Lupin, whether alone or in concert with a subsidiary company, from making, using, selling, offering for sale, and/or importing the Lupin ANDA Product or any pharmaceutical composition as claimed in the Patents-in-Suit in/into the United States, or practicing any processes or methods as claimed in the Patents-in-Suit, or from actively inducing or contributing to the infringement of any claim of the Patents-in-Suit, before the expiration of the Patents-in-Suit, inclusive of any extension(s) to patent term in accordance with 35 U.S.C. §§ 271(e)(4)(B) and 283;

(g) Damages or other monetary relief, including costs, fees, pre- and post-judgment interest, and damages under 35 U.S.C. § 271(e)(4)(C), to Plaintiffs if Lupin engages in commercial manufacture, use, offers to sell, sale, or importation in or into the United States of the Lupin ANDA Product prior to the latest expiration date of the Patents-in-Suit, including any extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled.

(h) To the extent the facts show that this is an exceptional case, an award of reasonable attorney fees in this action pursuant to 35 U.S.C. § 285;

(i) An award to Plaintiffs of any further appropriate relief under 35 U.S.C. § 271(e)(4);

(j) Costs and expenses in this action; and

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

Dated: February 17, 2023

Respectfully submitted,

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