UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

THERAVANCE BIOPHARMA R&D IP, LLC, THERAVANCE BIOPHARMA US, INC., THERAVANCE BIOPHARMA IRELAND LIMITED, MYLAN IRELAND LIMITED, and MYLAN SPECIALTY L.P.,	CIVIL ACTION No. _____ *Document Filed Electronically*
Plaintiffs, v. QILU PHARMACEUTICAL CO., LTD. and QILU PHARMA INC., Defendants.	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Theravance Biopharma R&D IP, LLC, Theravance Biopharma US, Inc., Theravance Biopharma Ireland Limited, Mylan Ireland Limited, and Mylan Specialty L.P. (collectively, "Plaintiffs"), by their attorneys, for their Complaint against Defendants Qilu Pharmaceutical Co., Ltd. and Qilu Pharma Inc. (collectively, "Defendants" or "Qilu"), 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"), 11,484,531 (the "'531 patent"), 11,691,948 (the "'948 patent"), and 11,858,898 (the "'898 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 No. 219523 (the "Qilu ANDA"), filed by Defendants, 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®, including the Patents-in-Suit.

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").

Defendants

11. On information and belief, Defendant Qilu Pharmaceutical Co., Ltd. is a company organized and existing under the laws of China, with its principal place of business at 8888 Lvyou Road, High-Tech Zone, Jinan, 250104, China.

12. On information and belief, Defendant Qilu Pharma Inc. is a company organized and existing under the laws of Pennsylvania, with its principal place of business at 101 Lindenwood Drive, Suite 225, Malvern, PA 19355.

13. On information and belief, Qilu Pharmaceutical Co., Ltd. and Qilu Pharma Inc. are in the business of, among other things, developing, preparing, manufacturing, selling, marketing, and distributing generic drugs, including distributing, selling, and marketing generic drugs throughout the United States, including within the Commonwealth of Pennsylvania, through their own actions and through the actions of their partners, agents, and subsidiaries, from which Qilu Pharmaceutical Co., Ltd. and Qilu Pharma Inc. derive a substantial portion of their revenue.

14. On information and belief, Qilu Pharmaceutical Co., Ltd. and Qilu Pharma Inc. acted in concert to prepare and submit the Qilu 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 Commonwealth of Pennsylvania, of a generic version of YUPELRI® (revefenacin) inhalation solution, for oral inhalation (the "Qilu ANDA Product"), prior to the expiration of the Patents-in-Suit.

15. On information and belief, following any FDA approval of the Qilu ANDA, Qilu Pharmaceutical Co., Ltd. and Qilu Pharma Inc. will act alone or in concert to commercially manufacture, import, market, offer for sale, distribute, and/or sell the Qilu ANDA Product throughout the United States, including within the Commonwealth of Pennsylvania.

JURISDICTION AND VENUE

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

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

18. 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.

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

20. This Court has personal jurisdiction over Qilu Pharma Inc. because, *inter alia*, Qilu Pharma Inc. is a corporation organized and existing under the laws of Pennsylvania, having its principal place of business within the Eastern District of Pennsylvania, at 101 Lindenwood Drive, Suite 225, Malvern, PA 19355.

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

22. This Court has personal jurisdiction over Defendants at least because, *inter alia*, on information and belief, (1) Qilu Pharmaceutical Co., Ltd. itself, and/or in concert with Qilu Pharma Inc., 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 Qilu ANDA Product in the United States, including the Commonwealth of Pennsylvania; and (2) Qilu Pharmaceutical Co., Ltd. itself, and/or in concert with Qilu Pharma Inc., will market, distribute, offer for sale, and/or sell the Qilu ANDA Product in the United States, including the Commonwealth of Pennsylvania, upon approval of ANDA No. 219523, and Defendants will derive substantial revenue from the use or consumption of the Qilu ANDA Product in the Commonwealth of Pennsylvania.

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

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

25. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1400(b) as to Qilu Pharma Inc. at least because, on information and belief, Qilu Pharma Inc. is incorporated under the laws of Pennsylvania. Further, on information and belief, Qilu maintains its principal place of business within the Eastern District of Pennsylvania, at 101 Lindenwood Drive, Suite 225,

Malvern, PA 19355. Thus, the Eastern District of Pennsylvania is "the judicial district where [Qilu Pharma Inc.] resides," and venue is proper pursuant to 28 U.S.C. § 1400(b).

26. Venue is proper in this judicial district because Qilu Pharma Inc. has a regular and established place of business in the Commonwealth of Pennsylvania, and at least because, on information and belief, Qilu Pharma Inc. has committed or aided, abetted, contributed to, and/or participated in the commission of, acts of infringement of the Patents-in-Suit that will lead to foreseeable harm and injury to Plaintiffs by preparing or assisting in preparing the Qilu ANDA in the Commonwealth of Pennsylvania and/or with the intention of seeking to market the Qilu ANDA Product nationwide, including within the Commonwealth of Pennsylvania.

THE PATENTS-IN-SUIT

The '451 Patent

27. 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.

28. 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.

29. The '451 patent is listed in the Orange Book as covering YUPELRI®.

The '028 Patent

30. 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.

31. 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.

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

The '081 Patent

33. 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.

34. 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.

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

The '289 Patent

36. 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.

37. 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.

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

The '531 Patent

39. 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.

40. 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.

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

The '948 Patent

42. The '948 patent, titled "Crystalline Freebase Forms of a Biphenyl Compound," was duly and legally issued by the USPTO on July 4, 2023. A true and correct copy of the '948 patent is attached as Exhibit F.

43. Theravance Biopharma R&D IP, LLC is the assignee of the '948 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '948 patent. Mylan Ireland Limited is the exclusive sub-licensee of the '948 patent from Theravance Biopharma Ireland Limited.

44. The '948 patent is listed in the Orange Book as covering YUPELRI®.

The '898 Patent

45. The '898 patent, titled "Crystalline Freebase Forms of a Biphenyl Compound," was duly and legally issued by the USPTO on January 2, 2024. A true and correct copy of the '898 patent is attached as Exhibit G.

46. Theravance Biopharma R&D IP, LLC is the assignee of the '898 patent. Theravance Biopharma Ireland Limited is the exclusive licensee of the '898 patent. Mylan Ireland Limited is the exclusive sub-licensee of the '898 patent from Theravance Biopharma Ireland Limited.

47. The '898 patent is listed in the Orange Book as covering YUPELRI®.

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 H 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. (Exhibit H 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%). (Exhibit H 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 2024.

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 May 6, 2024, purporting to be notice under 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 (the "Qilu Notice Letter"), Qilu purports to have notified Theravance Biopharma US, Inc., Theravance Biopharma R&D IP, LLC, Theravance Biopharma Ireland Limited, Mylan Specialty LP, Mylan Ireland Ltd., and Mylan Pharmaceuticals Inc. that it had submitted ANDA No. 219523 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 "Qilu ANDA Product"), as a generic version of YUPELRI® in/into the United States, prior to the expiration of the Patents-in-Suit.

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

64. Qilu filed the Qilu 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 Qilu ANDA Product.

65. The Qilu Notice Letter states that Qilu has attached a "detailed statement of the legal and factual basis" for Qilu's Paragraph IV certifications that, in its opinion, the Patents-in-Suit are invalid and/or not infringed by Qilu's ANDA Product. (Qilu Notice Letter at 3). Neither the Qilu Notice Letter nor its attached "detailed statement" provide any substantive invalidity allegation with respect to the '451 patent, '028 patent, '081 patent, '289 patent, '948 patent, and '898 patent.

66. In the Notice Letter, Qilu offered confidential access to portions of its ANDA No. 219523, on terms and conditions set forth in the Qilu Notice Letter (the "Qilu Offer"). Qilu requested that Plaintiffs accept the Qilu Offer before receiving access to the Qilu ANDA. The Qilu Offer contained restrictions that contravene 21 U.S.C. § 355(j)(5)(C)(i)(III).

67. On information and belief, the active ingredient of the Qilu 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.

68. On information and belief, Qilu asserts in ANDA No. 219523 that the Qilu ANDA Product is bioequivalent to YUPELRI®, refers to and relies upon the YUPELRI® NDA, and contains data that, according to Qilu, demonstrate the bioequivalence of the Qilu ANDA Product to YUPELRI®.

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

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

71. On information and belief, Qilu had knowledge of the Patents-in-Suit when it submitted and filed ANDA No. 219523.

72. On information and belief, Qilu 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. 219523 and prior to the expiration of the Patents-in-Suit.

73. On information and belief, Qilu will commercially manufacture, use, offer for sale, and/or sell the Qilu ANDA Product throughout the United States, import the Qilu 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.

74. On information and belief, Qilu knows that the Qilu 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, Qilu 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.

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

76. On information and belief, the Qilu 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.

77. The Qilu 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.

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

79. This action is being commenced within 45 days of receipt of the Qilu Notice Letter.

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

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

81. Qilu's submission of ANDA No. 219523 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 Qilu 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).

82. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu 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.

83. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu 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).

84. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '451 patent.

85. On information and belief, Qilu had knowledge of the '451 patent when it submitted ANDA No. 219523. Qilu's infringement has been, and continues to be, deliberate.

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

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

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

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

89. Qilu's submission of ANDA No. 219523 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 Qilu 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).

90. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu 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.

91. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '028 patent.

92. On information and belief, Qilu had knowledge of the '028 patent when it submitted ANDA No. 219523. Qilu's infringement has been, and continues to be, deliberate.

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

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

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

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

96. Qilu's submission of ANDA No. 219523 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 Qilu 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).

97. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu 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.

98. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '081 patent.

99. On information and belief, Qilu had knowledge of the '081 patent when it submitted ANDA No. 219523. Qilu's infringement has been, and continues to be, deliberate.

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

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

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

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

103. Qilu's submission of ANDA No. 219523 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 Qilu 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).

104. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu 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).

105. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '289 patent.

106. On information and belief, Qilu had knowledge of the '289 patent when it submitted ANDA No. 219523. Qilu's infringement has been, and continues to be, deliberate.

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

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

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

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

110. Qilu's submission of ANDA No. 219523 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 Qilu 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).

111. Unless enjoined, upon FDA approval of Qilu's ANDA No. 219523, Qilu will infringe one or more claims of the '531 patent by actively inducing infringement by others under 35 U.S.C. § 271(b).

112. On information and belief, upon FDA approval of Qilu's ANDA No. 219523, Qilu intends to manufacture, market, sell, and offer to sell Qilu's ANDA Product with an FDA-approved package insert that will direct healthcare providers and patients in the use of Qilu's ANDA Product.

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

114. 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.

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

116. 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).

117. 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®.

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

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

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

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

122. The "Dosage and Administration" section of the YUPELRI® package insert 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." (Exhibit H at § 2).

123. 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." (Exhibit H at § 3).

124. 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%.

125. The YUPELRI® package insert describes the treatment of moderate to very severe patients in Clinical Studies. (Exhibit H at § 14.2).

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

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

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

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

130. The GOLD guidelines, such as at pages 54-55, advise healthcare providers to check the patient's ability to use an inhaler.

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

132. 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.

133. On information and belief, Qilu specifically intends that the Qilu 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.

134. On information and belief, Qilu 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%.

135. On information and belief, Qilu 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%.

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

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

COUNT VI
INFRINGEMENT OF U.S. PATENT NO. 11,691,948 BY QILU

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

139. Qilu's submission of ANDA No. 219523 to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Qilu ANDA Product in/into the United States prior to the expiration of the '948 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '948 patent under 35 U.S.C. § 271(e)(2)(A).

140. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu ANDA Product into the United States, during the term of the '948 patent would infringe one or more claims of the '948 patent under 35 U.S.C. § 271(a), either literally or under the doctrine of equivalents.

141. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu ANDA Product into the United States, during the term of the '948 patent would infringe one or more claims of the '948 patent under 35 U.S.C. § 271(g).

142. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '948 patent.

143. On information and belief, Qilu had knowledge of the '948 patent when it submitted the Qilu '948 Patent Paragraph IV Certification as part of ANDA No. 219523. Qilu's infringement has been, and continues to be, deliberate.

144. Plaintiffs will be substantially and irreparably harmed if Qilu's infringement of the '948 patent is not enjoined.

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

COUNT VII
INFRINGEMENT OF U.S. PATENT NO. 11,858,898 BY QILU

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

147. Qilu's submission of ANDA No. 219523 to obtain approval from the FDA to engage in the commercial manufacture, importation, use, offer for sale, and/or sale of the Qilu ANDA Product in/into the United States prior to the expiration of the '898 patent constitutes infringement, either literally or under the doctrine of equivalents, of one or more claims of the '898 patent under 35 U.S.C. § 271(e)(2)(A).

148. Qilu's commercial manufacture, sale, offer for sale, or use of the Qilu ANDA Product within the United States, or importation of the Qilu ANDA Product into the United States, during the term of the '898 patent would infringe and/or induce infringement of one or more claims of the '898 patent under 35 U.S.C. §§ 271(a) and/or (b), either literally or under the doctrine of equivalents.

149. On information and belief, Qilu intends to engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Qilu ANDA Product, and the proposed labeling therefor, immediately and imminently upon the approval of ANDA No. 219523 and any amendments thereto, *i.e.*, prior to the expiration of the '898 patent.

150. On information and belief, Qilu has knowledge of the '898 patent. Qilu's infringement has been, and continues to be, deliberate.

151. Plaintiffs will be substantially and irreparably harmed if Qilu's infringement of the '898 patent is not enjoined.

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

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

(a) A judgment under 35 U.S.C. § 271(e)(2)(A) that Qilu has infringed one or more claims of the Patents-in-Suit by the filing of its ANDA No. 219523;

(b) A judgment that Qilu's manufacturing, using, selling, offering for sale, and/or importing the Qilu ANDA Product in/into the United States will infringe one or more claims 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 Qilu, 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 Qilu 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. 219523 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 Patents-in-Suit, 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 Qilu, 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 Qilu 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 Qilu, whether alone or in concert with a subsidiary company, from making, using, selling, offering for sale, and/or importing the Qilu 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 Qilu engages in commercial manufacture, use, offers to sell, sale, or importation in or into the United States of the Qilu 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: June 18, 2024

Respectfully submitted

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