IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NEXUS PHARMACEUTICALS, LLC, Plaintiff, v. HIKMA PHARMACEUTICALS USA INC. AND HIKMA PHARMACEUTICALS PLC, Defendants.	C.A. No. **JURY TRIAL DEMANDED**

COMPLAINT

Plaintiff Nexus Pharmaceuticals, LLC ("Nexus"), by and through its undersigned attorneys, for its Complaint against Defendants Hikma Pharmaceuticals USA Inc. ("Hikma USA") and Hikma Pharmaceuticals PLC ("Hikma PLC") (collectively "Defendants" or "Hikma") alleges as follows.

NATURE OF THE ACTION

1. This is an action under the patent laws of the United States, 35 U.S.C. § 1 *et seq.* and the Declaratory Judgment Act, 28 U.S.C. § 2201 *et seq.*, for patent infringement by Defendants of U.S. Patent Nos. 11,464,752 ("the '752 patent"), 11,426,369 ("the '369 patent"), and 11,571,398 ("the '398 patent") (collectively, "Patents-In-Suit") based upon a real, immediate, substantial, and justiciable controversy between the parties.

2. The act of infringement relates to Defendants' ongoing and/or imminent manufacture, use, sale, importation, offer to sell and/or active inducement or encouragement of others to do any of the foregoing, within the United States, of an ephedrine sulfate 25 mg/5 mL (5 mg/mL) solution in a prefilled-syringe presentation before expiration of the Patents-In-Suit.

THE PARTIES

3. Nexus is a corporation organized and existing under the laws of the State of Illinois, having its principal place of business at 400 Knightsbridge Parkway, Lincolnshire, Illinois 60069. Nexus has recently undergone a name change to Nexus Pharmaceuticals, LLC, a continuing entity recently registered that stands entirely in the place of Nexus Pharmaceuticals, Inc. By operation of Illinois law, all assets and operations of Nexus Pharmaceuticals, Inc. have now converted and merged into Nexus Pharmaceuticals, LLC.

4. Nexus is the holder of New Drug Application ("NDA") No. 213407 for EMERPHED®, (ephedrine sulfate) 50mg/10ml (5 mg/mL) IV solution. EMERPHED® was the first FDA-approved "ready-to-use" formulation for ephedrine sulfate. A ready-to-use formulation of ephedrine sulfate has a concentration of 5 mg/mL and does not require dilution before administration to a patient.

5. Nexus applied for and obtained patents for its inventions related to ready-to-use formulations for 5 mg/mL ephedrine sulfate, including the Patents-In-Suit. Nexus is the owner and assignee of the Patents-In-Suit.

6. On information and belief, Hikma USA is a corporation organized and existing under the laws of the state of Delaware with a principal place of business at 200 Connell Drive, 4th Floor, Berkeley Heights, New Jersey 07922.

7. On information and belief, Hikma PLC is a corporation organized and existing under the laws of the United Kingdom with its principal place of business at 1 New Burlington Place, London, W1S 2HR, United Kingdom.

8. On information and belief, Hikma USA is a wholly owned subsidiary of Hikma PLC.

9. On information and belief, Hikma USA acts at the direction, and for the benefit, of Hikma PLC, and is controlled and/or dominated by Hikma PLC.

10. On information and belief, Defendants collaborate with respect to the development, regulatory approval, marketing, sale, and/or distribution of pharmaceutical products, including generic pharmaceutical products, in the state of Delaware and throughout the United States. On further information and belief, Defendants are agents of each other and/or operate in concert as integrated parts of the same business group and enter into agreements with each other that are nearer than arm's length.

11. On information and belief, Hikma PLC and Hikma USA hold themselves out as a single entity for the purpose of manufacturing, selling, marketing, distribution, and importation of generic drug products.

JURISDICTION AND VENUE

12. This action arises under 35 U.S.C. § 1 *et seq.* generally and 35 U.S.C. § 271 specifically, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 et seq.

13. This Court has subject matter jurisdiction over this dispute pursuant to 28 U.S.C. §§ 1331 and 1338(a), because this action involves substantial claims arising under the United States Patent Act (35 U.S.C. § 1 et seq.). Jurisdiction is also based on the Federal Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, based on an actual and continuing controversy between the parties concerning the Patents-In-Suit as detailed below.

14. This Court has personal jurisdiction over Hikma USA because Hikma USA is a corporation organized and existing under the laws of the state of Delaware.

15. This Court also has personal jurisdiction over Hikma USA because this suit arises out of and relates to its activities that are, and will be, directed to the State of Delaware. On information and belief, Hikma USA has obtained approval from the Federal Food and Drug

Administration ("FDA") for an ephedrine sulfate 25 mg/5 mL (5 mg/mL) product under ANDA No. 217721, and has commenced manufacturing, marketing, and sale of that product, which is the subject of the infringement claims in this action, in the State of Delaware and throughout the United States, including in this judicial district.

16. Venue is proper in this District with respect to Hikma USA pursuant to 28 U.S.C. §§ 1391 and 1400(b) because Hikma USA is a corporation organized and existing under the laws of the state of Delaware.

17. On information and belief, Hikma USA and Hikma PLC acted collaboratively to obtain approval from the Federal Food and Drug Administration ("FDA") for an ephedrine sulfate 25 mg/5 mL (5 mg/mL) product under ANDA No. 217721 and have acted collaboratively to commence manufacturing, marketing, and sale of an ephedrine sulfate 25 mg/5 mL (5 mg/mL) product under ANDA No. 217721, which is the subject of the infringement claims in this action, in the State of Delaware and throughout the United States, including in this judicial district. For this reason, this Court also has personal jurisdiction over Hikma PLC because this suit arises out of and relates to its activities that are, and will be, directed to the State of Delaware.

18. This Court also has personal jurisdiction over Hikma PLC because, on information and belief, Hikma PLC manufactures, imports, offers for sale, and sells pharmaceutical drugs that are sold in the United States, including in Delaware, and derives substantial income therefrom.

19. In the alternative, this court may exercise personal jurisdiction over Hikma PLC pursuant to Fed. R. Civ. P. 4(k)(2) because (a) Plaintiff's claims arise under federal law; (b) Hikma PLC has sufficient contact with the United States as a whole, including but not limited to marketing and/or selling generic pharmaceutical products that are distributed and sold

throughout the United States, such that this Court's exercise of jurisdiction over Hikma PLC satisfies due process.

20. Venue is proper in this District with respect to Hikma PLC Pursuant to 28 U.S.C. § 1391(c)(3) because Hikma PLC is not a resident of the United States.

NEXUS'S EMERPHED® PRODUCTS AND THE PATENTS-IN-SUIT

21. EMERPHED® is sold and marketed under NDA No. 213407, which was approved by the FDA as a 50 mg/10 mL single-dose vial in April 2020.

22. FDA later approved sNDA 213407-S004 for 25mg/5mL and 50mg/10mL single-dose pre-filled syringes on February 28, 2023.

23. Ephedrine, the active ingredient in EMERPHED®, is an alpha- and beta-adrenergic agonist and a norepinephrine-releasing agent. EMERPHED® is indicated for the treatment of clinically important hypotension occurring in the setting of anesthesia.

24. The '752 patent, entitled "Compositions Comprising Ephedrine Or An Ephedrine Salt And Methods Of Making And Using Same," was duly and legally issued on October 11, 2022. A true and correct copy of the '752 patent is attached hereto as Exhibit A.

25. The '752 patent stems from U.S. Application No. 17/381,770 ("the '770 application"), filed on July 21, 2021, which claims priority to U.S. Application No. 16/876,020, filed on May 16, 2020 (now U.S. Patent No. 11,090,278), and ultimately claims priority to U.S. Provisional Application No. 62/849,125, filed on May 16, 2019.

26. The '752 patent claims are directed to ready-to-use ephedrine sulfate composition products.

27. The '752 patent is valid and duly issued, and will not expire until at least May 16, 2040.

28. The ’369 patent, entitled “Compositions Comprising Ephedrine Or An Ephedrine Salt And Methods Of Making And Using Same,” was duly and legally issued on August 30, 2022. A true and correct copy of the ’369 patent is attached hereto as Exhibit B.

29. The ’369 patent stems from U.S. Application No. 17/556,904 (“the ’904 application”), filed on December 20, 2021, which claims priority to U.S. Application No. 17/381,770, filed on July 21, 2021, which in turn claims priority to U.S. Application No. 16/876,020, filed on May 16, 2020 (now U.S. Patent No. 11,090,278), and ultimately claims priority to U.S. Provisional Application No. 62/849,125, filed on May 16, 2019.

30. The ’369 patent claims are directed to a shelf-stable, ready to use ephedrine sulfate composition.

31. The ’369 patent is valid and duly issued, and will not expire until at least May 16, 2040.

32. The ’398 patent, entitled “Compositions Comprising Ephedrine Or An Ephedrine Salt And Methods Of Making And Using Same,” was duly and legally issued on February 7, 2023. A true and correct copy of the ’398 patent is attached hereto as Exhibit C.

33. The ’398 patent stems from U.S. Application No. 17/943,185 (“the ’185 application”), filed on September 12, 2022, which is a division of U.S. Application No. 17/381,770, filed on July 21, 2021 (now U.S. Pat. No. 11,464,752), which is a continuation of U.S. Application No. 16/876,020, filed on May 16, 2020 (now U.S. Pat. No. 11,090,278), and ultimately claims priority to U.S. Provisional Application No. 62/849,125, filed on May 16, 2019.

34. The ’398 patent claims are directed to methods of administering ready-to-use ephedrine sulfate composition products.

35. The '398 patent is valid and duly issued, and will not expire until at least May 16, 2040.

DEFENDANTS' PRODUCT AND INFRINGING CONDUCT

36. On information and belief, Defendants have obtained approval from the Federal Food and Drug Administration ("FDA") for an ephedrine sulfate 25 mg/5 mL (5 mg/mL) prefilled-syringe presentation product under Application No. 217721, an abbreviated new drug application under section 505(j) of the Federal Food, Drug, and Cosmetic Act ("Defendants' Product").

37. On the FDA's website, Defendants' Product is listed as a 25 mg/5 mL (5 mg/mL) ephedrine sulfate solution approved by the FDA on October 11, 2024, and "Hikma" is listed as the company that owns the product:

https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=217721

38. On information and belief, Hikma's prescribing information (label) is available online at https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=24787cb1-23e8-4baa-9838-a31a466b8c79&type=display. Attached as Exhibit D is Hikma's label as accessed from the foregoing website on January 2, 2025. On information and belief, Hikma's label indicates that Defendants' Product is available in a prefilled syringe.

39. Because Defendants' Product has been approved by FDA, Hikma can manufacture, has manufactured, offer for sale, and sell that product commercially in the United States and in this District.

40. On information and belief, Hikma began commercial marketing of Defendants' Product on or about December 20, 2024. At the end of its label for Defendants' Product, Hikma indicates that its "Marketing Start Date" was December 20, 2024. (Ex. D, *available at*

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=24787cb1-23e8-4baa-9838-a31a466b8c79&type=display).

41. On information and belief, Hikma's efforts to commercialize the Defendants' Product are constant and all-encompassing.

42. On information and belief, Hikma has manufactured, is currently manufacturing, or directing and controlling the manufacture of, and/or are actively preparing to manufacture or direct and control the manufacture of, and/or will imminently manufacture or direct and control the manufacture of, Defendants' Product, so that the product can be offered for sale and sold in the United States and in this District.

43. On information and belief, Hikma intends that, following manufacture of Defendants' Product, Hikma has or will sell, distribute, and/or direct the sale and distribution of Defendants' Product that is, or will be, manufactured by or at the direction of Hikma.

44. On information and belief, Hikma has offered for sale and sold Defendants' Product before the expiration of the Patents-In-Suit asserted in this action.

45. As set forth in Counts below, the manufacture of Defendants' Product infringes one or more claims of the Patents-In-Suit.

46. On information and belief, Hikma was aware of and tracked Nexus's '904 application, '770 application, and '185 application through prosecution at the United States Patent and Trademark Office.

47. On information and belief, Hikma has been aware of Nexus's issued '369 patent since August 30, 2022, Nexus's issued '752 patent since October 11, 2022, and Nexus's issued '398 patent since February 7, 2023. Hikma is at least aware of the Patents-in-Suit as of the filing

of this Complaint. Despite that knowledge of the Patents-In-Suit, Hikma has indicated no intent to stop its infringing activity described above.

COUNT I
INFRINGEMENT OF THE '752 PATENT

48. Nexus incorporates and realleges the foregoing paragraphs.

49. On information and belief, Hikma began commercial marketing of Defendants' Product on or about December 20, 2024.

50. On information and belief, Hikma manufactures, uses, sells, offers for sale or imports; and/or directs and controls the manufacture, use, sale, offer for sale or importation of, Defendants' Product for sale in the United States, and these acts directly and/or indirectly infringe one or more claims of the '752 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c), and/or (g).

51. Hikma's manufacture, use, sale, offer for sale or importation of; or direction and control of the manufacture, use, sale, offer for sale or importation, of Defendants' Product constitutes infringement of one or more claims of the '752 patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

52. On information and belief, the manufacture, use, sale, offer for sale or importation of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions constitutes direct infringement of the '752 patent.

53. On information and belief, the manufacture, use, sale, offer for sale or importation of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions are inducing infringement of the '752 patent.

54. On information and belief, the manufacture, use, sale, offer for sale or importation of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions are contributing to the infringement of the '752 patent.

55. The '752 patent has sixteen claims directed to a ready-to-use ephedrine sulfate pharmaceutical product.

56. As one example, independent claim 1 of the '752 patent is directed to:

> A pharmaceutical product comprising:
>
> > a packaged syringe containing a sterilized ready-to-use ephedrine composition comprising:
> >
> > > a packaged concentration of ephedrine sulfate of 5 mg/mL,
> > >
> > > 9 mg/mL sodium chloride,
> > >
> > > no preservative,
> > >
> > > water, and
> > >
> > > an initial pH level of about 4.5 to about 7; and
> >
> > having, after storage in the syringe at 25° C. and 60% relative humidity for 12 months or after storage at 40° C. and 75% relative humidity for 6 months:
> >
> > > a pH level within 0.5 pH units of the initial pH level,
> > >
> > > an ephedrine sulfate concentration of at least 95% of the packaged concentration, and
> > >
> > > a bacterial endotoxin level not more than 7 EU/mg.

57. Consistent with this claim, and based on publicly available information, and on information and belief, Defendants' Product meets each and every limitation of claim 1 of the '752 patent literally or equivalently, and Hikma directly and/or indirectly infringes that claim

under 35 U.S.C. § 271(a), (b), (c), and/or (g). On information and belief, Hikma directly infringes at least claim 1 of the '752 patent because Defendants' Product contains each component of the claim. On information and belief, Hikma indirectly infringes the '752 patent by actively, knowingly and intentionally aiding, abetting, directing, encouraging, or otherwise instructing third parties and knowingly inducing third parties, including contract manufacturers, to commit acts that constitute infringement of the '752 patent.

58. Each heading below provides a term from claim 1 of the '752 patent and associated sufficient basis from Defendants' Product Label (Exhibit D) for showing infringement of each claim term. It is fully expected that discovery will provide additional factual support and details.

A pharmaceutical product comprising:

a packaged syringe containing a sterilized ready-to-use ephedrine composition comprising:

a packaged concentration of ephedrine sulfate of 5 mg/mL,

59. The FDA-approved label of Defendants' Product provides that "Ephedrine sulfate injection, 25mg/5ml (5 mg/mL) in a pre-filled syringe, is a premixed formulation. Do not dilute prior to use." Exhibit D at Dosage and Administration, section 2.1. It is therefore ready to use, because it does not require dilution, and in fact the product label confirms it must not be further diluted before administration because it is already "premixed" for the syringe product. The approved labeling also provides that Defendants' Product is "ephedrine sulfate" in a "single-dose 5mL prefilled syringe." *Id*. at Dosage Forms and Strengths, section 3.

60. The FDA-approved label of Defendants' "Product Information" includes a section for "Packaging" that includes a "Package Description" that lists "10 in 1 CARTON" and "5mL in 1 SYRINGE, PLASTIC." The Product Instructions for Use of Prefilled Syringe depict

removing the syringe from a "plastic overwrap." Section 2.1 states that "The single-dose prefilled syringe is intended for use in one patient during one surgical procedure. Discard any unused portion." This indicates that each individual syringe container is individually sealed. Each syringe thus includes a packaged concentration of ephedrine sulfate.

61. The FDA-approved label of Defendants' Product provides that "Ephedrine Sulfate Injection, USP is a clear, colorless, sterile solution for intravenous injection." Exhibit D, Dosage Forms and Strengths. In addition, the composition inside the syringe must meet stringent FDA criteria concerning sterility. Sterility is important to protect the drug safety, because if a product is unsterile then the FDA will not approve it since a patient may get microbial or other contamination without required sterility assurances. By virtue of FDA approval of the Defendants Product, it has deployed a formulation approach that meets the claimed criteria of a product that is "sterilized."

62. Upon information and belief and given that Defendants' Product was approved by the FDA including to meet stringent FDA standards regarding sterility, the Defendants' Product is a ready-to-use, sterilized pharmaceutical composition as required by claim 1 of the '752 patent.

9 mg/mL sodium chloride, no preservative, water, and an initial pH level of about 4.5 to about 7

63. The FDA-approved label of Defendants' Product provides that "each mL of the 5 mL single-dose prefilled syringe contains 5 mg ephedrine sulfate . . . and 8.6 mg Sodium Chloride, USP in water for injection." "The pH range is 4.5 to 6.5." Exhibit D, section 11. The label makes no mention of a preservative. The release specifications for the Defendants' Product must therefore require all commercial syringes to meet this requirement, otherwise the FDA

would not have approved the labeling requirement. Because the entire labeled range of 4.5 to 6.5 falls within the claimed range of "about 4.5 to about 7."

> **having, after storage in the syringe at 25° C. and 60% relative humidity for 12 months or after storage at 40° C. and 75% relative humidity for 6 months:**
>
> > **a pH level within 0.5 pH units of the initial pH level,**
> >
> > **an ephedrine sulfate concentration of at least 95% of the packaged concentration, and**

64. Exhibit D does not explicitly indicate a range of pH variance or the ephedrine sulfate concentration at the claimed temperature and humidity parameters. However, to obtain FDA approval, maintaining pH and active ingredient concentration within a tight range is important in order to show to FDA that the pH level is consistent and stable and the product is effective. The pH-stability relationship is especially true for ephedrine sulfate. As Nexus explained in its patent, "[e]phedrine sulfate compositions are known to be susceptible to light, pH changes, and humidity." Exhibit B at 1:63-2:2.

65. Companies routinely submit two types of stability testing to the FDA. Stability testing means evaluating a product's properties—including potency—over time. One type of stability testing is real-time, meaning leaving the product at room temperature with standard humidity (and a common approach to test this condition is 25 degrees Celsius and 60% relative humidity). The other type of stability testing is accelerated, meaning raising the temperature and humidity (and a common approach to test this condition is 40 degrees Celsius and 75% relative humidity) to model the effect of a longer time duration than if the product had been stored at room temperature and standard humidity. While Defendants' FDA submission is not public, the patent claim language is consistent with the testing that Hikma itself likely already did, on information

and belief, in order to demonstrate the pH and stability maintenance, so that it could obtain FDA approval, both referring to the real-time room temperature testing (consistent with the claimed 25 degrees Celsius and 60% relative humidity) and to the accelerated testing (consistent with the claimed 40 degrees Celsius and 75% relative humidity). Whether or not Hikma did the testing to confirm the claimed pH stability, on information and belief Defendants' Product does in fact meet this limitation.

66. The FDA requires stringent controls and tests to make sure product potency is maintained, and for a drug like ephedrine sulfate that is pH-sensitive, that in turn means monitoring pH for purposes of product stability. On information and belief, therefore, Defendants' Product meets the stringent FDA requirement for injectable products that maintain a potency of 95%-105% of the product throughout its shelf life, and given that range, then Hikma infringes just as Nexus invented for the claimed formulation that meets this criteria. On information and belief, therefore, Defendants' Product maintains the pH within 0.5 pH units otherwise the pH will vary over time, and in turn will affect the product stability. Further, on information and belief, Defendants' Product maintains an ephedrine sulfate concentration of at least 95% of the packaged concentration in order to comply with the FDA requirements.

67. Upon information and belief and given that Defendants' Product is approved by the FDA including to meet stringent FDA standards regarding stability, Defendants Product meets the requirement for having a pH level within 0.5 units of the initial pH level and at least 95% of the ephedrine sulfate level—either literally or under the doctrine of equivalents—for the claimed temperature and humidity conditions.

a bacterial endotoxin level not more than 7 EU/mg.

68. Exhibit D does not explicitly indicate a bacterial endotoxin level for Defendants' Products. However, the FDA sets standards limiting the level of endotoxins, and thus, on information and belief, Hikma has conducted testing to determine endotoxin levels. On information and belief, discovery will reveal that Defendants' product has a bacterial endotoxin level not more than 7 EU/mg.

69. On information and belief, Hikma has no reasonable basis for believing that Defendants' Product will not infringe one or more valid claims of the '752 patent and no reasonable basis for believing that the infringed claims are invalid.

70. Hikma's manufacture, use, importation, sale, or offer for sale of Defendants' Product constitutes willful infringement.

71. This case is "exceptional," and Nexus is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

72. The acts of infringement by Hikma set forth above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

73. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, offering for sale, or selling Defendants' Product in the United States before expiration of the '752 patent.

COUNT II
DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '752 PATENT

74. Nexus incorporates and realleges the foregoing paragraphs.

75. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. §§ 100 *et seq.*, including 35 U.S.C. § 271(a), (b), (c), and/or (g), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

76. To the extent that Hikma contends that there has been no manufacture, use, sale, importation or offer for sale of Defendants' Product at this time, there is still an actual case or controversy such that the Court may entertain Nexus's request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

77. On information and belief, FDA's approval of Defendants' Product, coupled with Hikma's commercial activities in support of the imminent manufacture, importation and/or launch of Defendants' Product, including at least: (i) Hikma's application to the FDA for permission to market Defendants' Product; and (ii) Hikma's commitment to commercializing Defendants' Product, create an actual, immediate, and real controversy under the Declaratory Judgment Act that Hikma will directly infringe, actively induce, and/or contribute to the infringement of valid and enforceable claims of the '752 patent before the '752 patent's expiration in violation of 35 U.S.C. § 271(a), (b), (c), and/or (g).

78. On information and belief, Hikma has engaged in and will continue to engage in substantial activities in preparation to manufacture, use, sell, offer for sale, import and/or market Defendants' Product in the United States.

79. On information and belief, Hikma will imminently manufacture, use, import, sell, offer for sale; and/or direct and control the imminent manufacture, use, importation, sale, or offer for sale of, Defendants' Product in the United States, and these acts directly and/or indirectly will infringe one or more claims of the '752 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c), and/or (g).

80. Hikma's imminent manufacture, use, importation, sale, or offer for sale; and/or direction and control of the manufacture, use, importation, sale, or offer for sale, of Defendants'

Product will constitute infringement of one or more claims of the '752 patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

81. On information and belief, the imminent manufacture, use, importation, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions will constitute direct infringement of the '752 patent.

82. On information and belief, the imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions will constitute induced infringement of the '752 patent.

83. On information and belief, the imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions will constitute contributory infringement of the '752 patent.

84. The imminent acts of infringement by Hikma set forth above will cause Nexus substantial and irreparable harm for which it has no adequate remedy at law.

85. On information and belief, Hikma has no reasonable basis for believing that Defendants' Product will not infringe one or more valid claims of the '752 patent and no reasonable basis for believing that those claims are invalid.

86. Hikma's imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product will constitute willful infringement.

87. This case is "exceptional," and Nexus is entitled to an award of attorney fees under 35 U.S.C. § 285.

88. A judicial declaration of infringement is necessary and appropriate to resolve this controversy.

89. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, offering for sale, or selling Defendants' Product in the United States before expiration of the '752 patent.

COUNT III
INFRINGEMENT OF THE '752 PATENT UNDER § 271(e)(2)

90. Nexus incorporates and realleges the foregoing paragraphs.

91. Hikma's submission of ANDA No. 217721, and supplementations thereto, to the FDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act to obtain approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation in to the United States of Defendants' Product that is claimed in the '752 patent, constitutes an act of infringement under 35 U.S.C. § 271(e)(2).

92. On information and belief, Hikma has and/or will imminently manufacture, use, import, sell, offer for sale; and/or direct and control the imminent manufacture, use, importation, sale, or offer for sale of, Defendants' Product in the United States, and these acts directly and/or indirectly will infringe one or more claims of the '752 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c), and/or (g).

93. Hikma's current and/or imminent manufacture, use, importation, sale, or offer for sale; and/or direction and control of the manufacture use, importation, sale, or offer for sale, of Defendants' Product constitutes infringement of one or more claims of the '752 patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

94. On information and belief, the current and/or imminent manufacture, use, importation, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions constitutes direct infringement of the '752 patent.

95. On information and belief, the current and/or imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions constitutes induced infringement of the '752 patent.

96. On information and belief, the current and/or imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product is covered by the claims of the '752 patent, and one or more of Hikma's actions constitutes contributory infringement of the '752 patent.

97. On information and belief, unless enjoined by this Court, Hikma's manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of Defendants' Product with its proposed labelling, Hikma will infringe, either literally or under the doctrine of equivalents, one or more claims of the '752 patent.

98. On information and belief, Hikma has no reasonable basis for believing that Defendants' Product will not infringe one or more valid claims of the '752 patent and no reasonable basis for believing that the infringed claims are invalid.

99. This case is "exceptional," as that term is used in 35 U.S.C. § 285.

100. The acts of infringement by Hikma above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

101. Nexus is entitled to the relief provided by 35 U.S.C. § 271(e)(4)(A), (B), and/or (C) including statutory relief, injunctive relief, and/or damages.

COUNT IV
INFRINGEMENT OF THE '369 PATENT

102. Nexus incorporates and realleges the foregoing paragraphs.

103. On information and belief, Hikma began commercial marketing of Defendants' Product on or about December 20, 2024.

104. On information and belief, Hikma manufactures, and/or directs and controls the manufacture of, Defendants' Product for use, sale, or offer for sale in the United States, and/or imports Defendants' Product into the United States, and these acts directly and/or indirectly infringe one or more claims of the '369 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c), and/or (g).

105. Hikma's acts constitute infringement of one or more claims of the '369 patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

106. On information and belief, the manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions constitutes direct infringement of the '369 patent.

107. On information and belief, the manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions are inducing infringement of the '369 patent.

108. On information and belief, the manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions are contributing to the infringement of the '369 patent.

109. The '369 patent has nine claims directed to methods for making a shelf-stable, ready-to-use ephedrine sulfate composition.

110. As one example, independent claim 1 of the '369 patent is directed to:

> A method of making a shelf-stable, ready-to-use ephedrine sulfate composition, the method comprising:
>
> > combining ephedrine sulfate, sodium chloride or dextrose, and water to form a batch solution comprising an initial ephedrine sulfate level of 5 mg/mL, 9 mg/mL sodium chloride or 5% dextrose, and no preservative;

> optionally contacting the batch solution with an acid or a base to obtain an initial pH level of the solution of 4.5 to 7;
>
> filtering the batch solution through a membrane filter to obtain a filtered batch solution;
>
> sanitizing one or more containers;
>
> placing not more than 20 mL of the filtered batch solution into one of the one or more sanitized containers to obtain one or more filled containers;
>
> sealing each filled container to obtain sealed containers including a shelf-stable, ready-to-use ephedrine sulfate composition; and
>
> maintaining a pH level of the shelf-stable, ready-to-use ephedrine sulfate composition in the sealed containers that is within 0.5 pH units of the initial pH level during storage at 25° C. and 60% relative humidity for at least 12 months or during storage at 40° C. and 75% relative humidity for at least 6 months.

111. Consistent with this claim, and based on publicly available information, and on information and belief, the manufacture of Defendants' Product meets each and every limitation of claim 1 of the '369 patent literally or equivalently, and Hikma directly and/or indirectly infringe that claim under 35 U.S.C. § 271(a), (b), (c), and/or (g). On information and belief, Hikma directly infringes the claims of the '369 patent because each step of the claims is performed by and/or attributable to Hikma. On information and belief, Hikma indirectly infringes the '369 patent by actively, knowingly and intentionally aiding, abetting, directing, encouraging, or otherwise instructing third parties and knowingly inducing third parties, including contract manufacturers, to commit acts that constitute infringement of the '369 patent.

112. Each heading below provides a term from claim 1 of the '369 patent and associated sufficient basis from Defendants' Product Label (Exhibit D) for showing infringement

of each claim term. It is fully expected that discovery will provide additional factual support and details.

> **A method of making a shelf-stable, ready-to-use ephedrine sulfate composition, the method comprising:**
>
> > **combining ephedrine sulfate, sodium chloride or dextrose, and water to form a batch solution comprising an initial ephedrine sulfate level of 5 mg/mL, 9 mg/mL sodium chloride or 5% dextrose, and no preservative;**

113. The FDA-approved label of Defendants' Product provides that "Ephedrine sulfate injection, 25mg/5ml (5 mg/mL) in a pre-filled syringe, is a premixed formulation. Do not dilute prior to use." Exhibit D at Dosage and Administration, section 2.1. It is therefore ready to use, because it does not require dilution, and in fact the product label confirms it must not be further diluted before administration because it is already "premixed" for the syringe product. The approved labeling also provides that Defendants' Product is "ephedrine sulfate" in a "single-dose 5mL prefilled syringe." *Id.* at Dosage Forms and Strengths.

114. The FDA-approved label of Defendants' Product provides that "each mL of the 5 mL single-dose prefilled syringe contains 5 mg ephedrine sulfate . . . and 8.6 mg Sodium Chloride, USP in water for injection." Exhibit D, section 11. The label makes no mention of a preservative.

115. Exhibit D does not provide the complete details of Hikma's manufacturing process. Pharmaceutical manufacturing is commonly accomplished by creating large batches of solutions combining ingredients, and then providing a conveyor belt approach to fill individual vials from those large batches. It is not always known unless and until someone invents a formulation whether or not it will work for its intended purpose. But now that Nexus has

demonstrated through its invention that its claimed formulation can be made, on information and belief, Hikma uses this same general manufacturing process to make Defendants' Product.

116. On information and belief, Defendants' Product is very likely manufactured to make vials containing ephedrine sulfate and sodium chloride by first making a batch solution with those concentrations, and then dispensing the batch into individual vials. Otherwise, they would have to manually prepare formulations in each individual syringe one at a time, which is inefficient and costly for an FDA-approved manufactured process.

117. The composition inside the syringe must meet stringent FDA criteria to maintain the shelf life for the duration of the product, while remaining stable. Stability is important to protect the drug potency, because if a product is unstable then the FDA will not approve it since a patient may not get the proper amount of ephedrine sulfate. On information and belief, Defendants' Product, which is FDA approved, has deployed a formulation approach that meets the claimed criteria of a product that is "shelf-stable."

optionally contacting the batch solution with an acid or a base to obtain an initial pH level of the solution of 4.5 to 7;

118. This claim limitation references an "optional[]" step so is not required to show infringement. Hikma reports, however, that it does use this step.

119. Exhibit D states that pH is "adjusted with Sodium Hydrochloride, NF. The pH range is 4.5 to 6.5."

filtering the batch solution through a membrane filter to obtain a filtered batch solution;

120. As Nexus reported in its patent, the batch solution was "filtered through Opticap® XL4 Durapore® non-fiber releasing membrane filter membranes" before dispersing into

containers. Exhibit B at 17:59-18:2. This filtering step helps to remove impurities and other particles from the batch solution before it is dispersed into vials or syringes.

121. Exhibit D does not provide the complete details of Hikma's manufacturing process. However, upon information and belief and given that the Defendants' Product is approved by the FDA including to meet stringent FDA standards regarding impurities and other contaminants within individual syringes, Hikma filters Defendants' Product to obtain a filtered batch solution or performs an equivalent sterilization step.

sanitizing one or more containers;

122. Nexus invented a suitable formulation for FDA approval, including to sanitize individual containers—whether vials or syringes—to achieve a safe and effective product that can be reliably used in the industry.

123. Exhibit D does not provide the complete details of Hikma's manufacturing process. However, upon information and belief and given that the Defendants' Product is approved by the FDA including to meet stringent FDA standards regarding impurities and other contaminants within individual syringes, Hikma sanitizes the syringe containers it uses for Defendants' Product.

placing not more than 20 mL of the filtered batch solution into one of the one or more sanitized containers to obtain one or more filled containers;

124. The approved labeling for Defendants' Product provides that it is a "5 mL single-dose prefilled syringe." Exhibit D at section 11. As 5 mL is less than 20 mL, and each syringe contains 5 mL in the syringe, Hikma places not more than 20 mL of the filtered batch into the syringe containers.

sealing each filled container to obtain sealed containers including a shelf-stable, ready-to-use ephedrine sulfate composition; and

maintaining a pH level of the shelf-stable, ready-to-use ephedrine sulfate composition in the sealed containers that is within 0.5 pH units of the initial pH level during storage at 25° C. and 60% relative humidity for at least 12 months or during storage at 40° C. and 75% relative humidity for at least 6 months.

125. Hikma sells individual syringes, which meet stringent FDA criteria for safety and efficacy as to each individual unit. As Hikma instructs on the Defendants' Product label, "The single-dose prefilled syringe is intended for use in one patient during one surgical procedure. Discard any unused portion" Exhibit D at Section 2.1. This indicates that each individual syringe container is individually sealed. For at least these reasons, on information and belief, Defendants' Product meets the "sealing" step for each individual syringe container.

126. The composition inside the syringe must meet stringent FDA criteria to maintain the shelf life for the duration of the product, while remaining stable. Stability is important to protect the drug potency, because if a product is unstable then the FDA will not approve it since a patient may not get the proper amount of ephedrine sulfate. On information and belief, Defendants' Product, which is FDA approved, has deployed a formulation approach that meets the claimed criteria of a product that is "shelf-stable."

127. The FDA-approved label of Defendants' Product provides that "Ephedrine sulfate injection, 25mg/5ml (5 mg/mL) in a pre-filled syringe, is a premixed formulation. Do not dilute prior to use." Exhibit D at Dosage and Administration, section 2.1. It is therefore ready to use, because it does not require dilution, and in fact the product label confirms it must not be further diluted before administration because it is already "premixed" for the syringe product. The

approved labeling also provides that Defendants' Product is "ephedrine sulfate" in a "single-dose 5mL prefilled syringe." *Id*. at Dosage Forms and Strengths.

128. The composition inside the syringe must meet stringent criteria to maintain a pH as specified on the product label itself. The Defendants' Product label provides that the pH range of the syringe product must be between 4.5 to 6.5. Exhibit D at section 11. Exhibit D does not explicitly indicate a range of pH variance or the ephedrine sulfate concentration at the claimed temperature and humidity parameters. However, to obtain FDA approval, maintaining pH and active ingredient concentration within a tight range is important in order to show to FDA that the pH level is consistent and stable and the product is effective. The pH-stability relationship is especially true for ephedrine sulfate. As Nexus explained in its patent, "[e]phedrine sulfate compositions are known to be susceptible to light, pH changes, and humidity." Exhibit B at 1:63-2:2.

129. Companies routinely submit two types of stability testing to the FDA. Stability testing means evaluating a product's properties—including potency—over time. One type of stability testing is real-time, meaning leaving the product at room temperature with standard humidity (and a common approach to test this condition is 25 degrees Celsius and 60% relative humidity). The other type of stability testing is accelerated, meaning raising the temperature and humidity (and a common approach to test this condition is 40 degrees Celsius and 75% relative humidity) to model the effect of a longer time duration than if the product had been stored at room temperature and standard humidity. While Defendants' FDA submission is not public, the patent claim language is consistent with the testing that Hikma itself likely already did, on information and belief, in order to demonstrate the pH and stability maintenance, so that it could obtain FDA approval, both referring to the real-time room temperature testing (consistent with the claimed 25 degrees Celsius and 60% relative humidity) and to the accelerated testing (consistent with the

claimed 40 degrees Celsius and 75% relative humidity). Whether or not Hikma did the testing to confirm the claimed pH stability, on information and belief Defendants' Product does in fact meet this limitation.

130. The FDA requires stringent controls and tests to make sure product potency is maintained, and for a drug like ephedrine sulfate that is pH-sensitive, that in turn means monitoring pH for purposes of product stability. On information and belief, therefore, Defendants' Product meets the stringent FDA requirement for injectable products that maintain a potency of 95%-105% of the product throughout its shelf life, and given that range, then Hikma infringes just as Nexus invented for the claimed formulation that meets this criteria. On information and belief, therefore, Defendants' Product maintains the pH within 0.5 pH units otherwise the pH will vary over time, and in turn will affect the product stability.

131. Upon information and belief and given that Defendants' Product is approved by the FDA including to meet stringent FDA standards regarding stability, Defendants Product meets the requirement for maintaining a pH level within 0.5 units of the initial pH level—either literally or under the doctrine of equivalents—for the claimed temperature and humidity conditions.

132. On information and belief, Hikma has no reasonable basis for believing that Defendants' Product will not infringe one or more valid claims of the '369 patent and no reasonable basis for believing that the infringed claims are invalid.

133. Hikma's manufacture of Defendants' Product constitutes willful infringement.

134. This case is "exceptional," and Nexus is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

135. The acts of infringement by Hikma set forth above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

136. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, offering for sale, or selling Defendants' Product in the United States before expiration of the '369 patent.

COUNT V
DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '369 PATENT

137. Nexus incorporates and realleges the foregoing paragraphs.

138. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. §§ 100 *et seq.*, including 35 U.S.C. § 271(a), (b), (c), and/or (g), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

139. To the extent that Hikma contends that there has been no manufacture and/or importation of Defendants' Product at this time, there is still an actual case or controversy such that the Court may entertain Nexus's request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

140. On information and belief, FDA's approval of Defendants' Product, coupled with Hikma's commercial activities in support of the imminent manufacture, importation and/or launch of Defendants' Product, including at least: (i) Hikma's application to the FDA for permission to market Defendants' Product; and (ii) Hikma's commitment to commercializing Defendants' Product, create an actual, immediate, and real controversy under the Declaratory Judgment Act that Hikma will directly infringe, actively induce, and/or contribute to the

infringement of valid and enforceable claims of the '369 patent before the '369 patent's expiration in violation of 35 U.S.C. § 271(a), (b), (c), and/or (g).

141. On information and belief, Hikma has engaged in and will continue to engage in substantial activities in preparation to manufacture and market Defendants' Product in the United States.

142. On information and belief, Hikma will imminently manufacture, or direct and control the imminent manufacture of, Defendants' Product for sale in the United States, and these acts directly and/or indirectly will infringe one or more claims of the '369 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(a), (b), (c), and/or (g).

143. Hikma's imminent manufacture, or direction and control of the manufacture, of Defendants' Product will constitute infringement of one or more claims of the '369 patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

144. On information and belief, the imminent manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions will constitute direct infringement of the '369 patent.

145. On information and belief, the imminent manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions will constitute induced infringement of the '369 patent.

146. On information and belief, the imminent manufacture of Defendants' Product is covered by the claims of the '369 patent, and one or more of Hikma's actions will constitute contributory infringement of the '369 patent.

147. The imminent acts of infringement by Hikma set forth above will cause Nexus substantial and irreparable harm for which it has no adequate remedy at law.

148. On information and belief, Hikma has no reasonable basis for believing that Defendants' Product will not infringe one or more valid claims of the '369 patent and no reasonable basis for believing that those claims are invalid.

149. Hikma's imminent manufacture of Defendants' Product will constitute willful infringement.

150. This case is exceptional, and Nexus is entitled to an award of attorney fees under 35 U.S.C. § 285.

151. A judicial declaration of infringement is necessary and appropriate to resolve this controversy.

152. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, offering for sale, or selling Defendants' Product in the United States before expiration of the '369 patent.

COUNT VII
INFRINGEMENT OF THE '398 PATENT

153. Nexus incorporates and realleges the foregoing paragraphs.

154. On information and belief, Hikma began commercial marketing of Defendants' Product on or about December 20, 2024.

155. On information and belief, Hikma has engaged in and will continue to engage in substantial activities in preparation to manufacture, market, sell and offer to sell Defendants' Product in the United States

156. On information and belief, Hikma manufactures, uses, sells, offers for sale or imports; and/or directs and controls the manufacture, use, sale, offer for sale or importation of, Defendants' Product for sale in the United States with an FDA-approved package insert that will direct healthcare providers and patients in the use of Defendants' Product, and these acts

indirectly infringe one or more claims of the '398 patent literally and/or under the doctrine of equivalents under 35 U.S.C. § 271 (b) or (c).

157. A healthcare provider has directly infringed, either literally or under the doctrine of equivalents, one or more of the claims of the '398 patent. Specifically, on information and belief, a healthcare provider administering Defendants' Product in accordance with the Defendants' Product package insert, has performed all of the steps of one or more claims of the '398 patent.

158. On information and belief, Hikma, currently does and/or previously did, actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hikma knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent by marketing Defendants' Product with the FDA-approved package insert.

159. The '398 patent has nine claims directed to a method of administering a ready-to-use ephedrine sulfate pharmaceutical product.

160. As one example, independent claim 1 of the '398 patent is directed to:

> A method of administering ephedrine to a subject having hypotension or at risk of developing hypotension in need thereof, the method comprising:
>
> > removing, from sealed packaging, a syringe containing a sterilized ready-to-use ephedrine composition comprising:
> >
> > > a packaged concentration of ephedrine sulfate of 5 mg/mL,
> > >
> > > 9 mg/mL sodium chloride or 5% dextrose,
> > >
> > > no preservative,
> > >
> > > water, and

an initial pH level of about 4.5 to about 7; and

having, after storage in the syringe at 25° C. and 60% relative humidity for 12 months or after storage at 40° C. and 75% relative humidity for 6 months:

a pH level within 0.5 pH units of the initial pH level,

an ephedrine sulfate concentration of at least 95% of the packaged concentration, and

a bacterial endotoxin level not more than 7 EU/mg.

injecting the sterilized ephedrine composition from the syringe into the subject without diluting the sterilized ephedrine composition.

161. Consistent with this claim, and based on publicly available information, and on information and belief, a healthcare provider has directly infringed one of more of the claims of the ’398 patent. Specifically, a healthcare provider administering Defendants’ Product in accordance with Hikma’s package insert has performed all of the steps of one or more claims of the ’398 patent.

162. Each heading below provides a term from claim 1 of the ’398 patent and associated sufficient basis from Defendants’ Product Label (Exhibit D) for showing infringement of each claim term. It is fully expected that discovery will provide additional factual support and details.

A method of administering ephedrine to a subject having hypotension or at risk of developing hypotension in need thereof, the method comprising:

163. The Indications and Usage section of Exhibit D states “Ephedrine sulfate injection is indicated for the treatment of important hypotension occurring in the setting of anesthesia.”

Section 2.4 provides "Instructions for Use of Prefilled Syringe." On information and belief, healthcare providers will follow the instructions provided by Hikma in Exhibit D and administer Defendants' Product to a patient having hypotension or at risk of developing hypotension.

> **removing, from sealed packaging, a syringe containing a sterilized ready-to-use ephedrine composition comprising:**
>
> > **a packaged concentration of ephedrine sulfate of 5 mg/mL,**
> >
> > **9 mg/mL sodium chloride or 5% dextrose,**
> >
> > **no preservative,**
> >
> > **water, and**
> >
> > **an initial pH level of about 4.5 to about 7; and**

164. Section 2.4 of Exhibit D instructs the healthcare provider to "Remove the syringe from the plastic overwrap."

165. Hikma sells individual syringes, which meet stringent FDA criteria for safety and efficacy as to each individual unit. As Hikma instructs on the Defendants' Product label, "The single-dose prefilled syringe is intended for use in one patient during one surgical procedure. Discard any unused portion" Exhibit D at Section 2.1. This indicates that each individual syringe container is individually sealed. For at least these reasons, on information and belief, to administer Defendants' Product, the healthcare provider must remove it from sealed packaging.

166. The FDA-approved label of Defendants' Product provides that "Ephedrine sulfate injection, 25mg/5ml (5 mg/mL) in a pre-filled syringe, is a premixed formulation. Do not dilute prior to use." Exhibit D at Dosage and Administration, section 2.1. It is therefore ready to use, because it does not require dilution, and in fact the product label confirms it must not be further

diluted before administration because it is already "premixed" for the syringe product. The approved labeling also provides that Defendants' Product is "ephedrine sulfate" in a "single-dose 5mL prefilled syringe." *Id*. at Dosage Forms and Strengths.

167. The FDA-approved label of Defendants' "Product Information" includes a section for "Packaging" that includes a "Package Description" that lists "10 in 1 CARTON" and "5mL in 1 Syringe." The Product Instructions for Use of Prefilled Syringe depict removing the syringe from a "plastic overwrap." Section 2.1 states that "The single-dose prefilled syringe is intended for use in one patient during one surgical procedure. Discard any unused portion." This indicates that each individual syringe container is individually sealed. Each syringe thus includes a packaged concentration of ephedrine sulfate.

168. The FDA-approved label of Defendants' Product provides that "Ephedrine Sulfate Injection, USP is a clear, colorless, sterile solution for intravenous injection." Exhibit D, Dosage Forms and Strengths. In addition, the composition inside the syringe must meet stringent FDA criteria concerning sterility. Sterility is important to protect the drug safety, because if a product is unsterile then the FDA will not approve it since a patient may get microbial or other contamination without required sterility assurances. By virtue of FDA approval of the Defendants Product, it has deployed a formulation approach that meets the claimed criteria of a product that is "sterilized."

169. Upon information and belief and given that Defendants' Product was approved by the FDA including to meet stringent FDA standards regarding sterility, the Defendants Product is a ready-to-use, sterilized pharmaceutical composition as required by claim 1 of the '752 patent.

170. The FDA-approved label of Defendants' Product provides that "each mL of the 5 mL single-dose prefilled syringe contains 5 mg ephedrine sulfate . . . and 8.6 mg Sodium

Chloride, USP in water for injection." "The pH range is 4.5 to 6.5." Exhibit D, section 11. The label makes no mention of a preservative. The release specifications for the Defendants' Product must therefore require all commercial syringes to meet this requirement, otherwise the FDA would not have approved the labeling requirement. Because the entire labeled range of 4.5 to 6.5 falls within the claimed range of "about 4.5 to about 7."

> **having, after storage in the syringe at 25° C. and 60% relative humidity for 12 months or after storage at 40° C. and 75% relative humidity for 6 months:**
>
> > **a pH level within 0.5 pH units of the initial pH level,**
> >
> > **an ephedrine sulfate concentration of at least 95% of the packaged concentration, and**
> >
> > **a bacterial endotoxin level not more than 7 EU/mg.**

171. Exhibit D does not explicitly indicate a range of pH variance or the ephedrine sulfate concentration at the claimed temperature and humidity parameters. However, to obtain FDA approval, maintaining pH and active ingredient concentration within a tight range is important in order to show to FDA that the pH level is consistent and stable and the product is effective. The pH-stability relationship is especially true for ephedrine sulfate. As Nexus explained in its patent, "[e]phedrine sulfate compositions are known to be susceptible to light, pH changes, and humidity." Exhibit B at 1:63-2:2.

172. Companies routinely submit two types of stability testing to the FDA. Stability testing means evaluating a product's properties—including potency—over time. One type of stability testing is real-time, meaning leaving the product at room temperature with standard humidity (and a common approach to test this condition is 25 degrees Celsius and 60% relative

humidity). The other type of stability testing is accelerated, meaning raising the temperature and humidity (and a common approach to test this condition is 40 degrees Celsius and 75% relative humidity) to model the effect of a longer time duration than if the product had been stored at room temperature and standard humidity. While Defendants' FDA submission is not public, the patent claim language is consistent with the testing that Hikma itself likely already did, on information and belief, in order to demonstrate the pH and stability maintenance, so that it could obtain FDA approval, both referring to the real-time room temperature testing (consistent with the claimed 25 degrees Celsius and 60% relative humidity) and to the accelerated testing (consistent with the claimed 40 degrees Celsius and 75% relative humidity). Whether or not Hikma did the testing to confirm the claimed pH stability, on information and belief Defendants' Product does in fact meet this limitation.

173. The FDA requires stringent controls and tests to make sure product potency is maintained, and for a drug like ephedrine sulfate that is pH-sensitive, that in turn means monitoring pH for purposes of product stability. On information and belief, therefore, Defendants' Product meets the stringent FDA requirement for injectable products that maintain a potency of 95%-105% of the product throughout its shelf life, and given that range, then Hikma infringes just as Nexus invented for the claimed formulation that meets this criteria. On information and belief, therefore, Defendants' Product maintains the pH within 0.5 pH units otherwise the pH will vary over time, and in turn will affect the product stability. Further, on information and belief, Defendants' Product maintains an ephedrine sulfate concentration of at least 95% of the packaged concentration in order to comply with the FDA requirements.

174. Upon information and belief and given that Defendants' Product is approved by the FDA including to meet stringent FDA standards regarding stability, Defendants Product

meets the requirement for having a pH level within 0.5 units of the initial pH level and at least 95% of the ephedrine sulfate level—either literally or under the doctrine of equivalents—for the claimed temperature and humidity conditions.

175. Exhibit D does not explicitly indicate a bacterial endotoxin level for Defendants' Products. However, the FDA sets standards limiting the level of endotoxins, and thus, on information and belief, Hikma has conducted testing to determine endotoxin levels. On information and belief, discovery will reveal that Defendants' product has a bacterial endotoxin level not more than 7 EU/mg.

injecting the sterilized ephedrine composition from the syringe into the subject without diluting the sterilized ephedrine composition.

176. The FDA-approved label of Defendants' Product provides detailed instructions for the healthcare provider to administer the medication by injection. Exhibit D, section 2.4, Instructions for Use of Prefilled Syringe. Those instructions include "Connect the syringe to an appropriate intravenous connection" and "Depress plunger rod to deliver medication." On information and belief, the healthcare providers follow the instructions for administration in the FDA-approved label of Defendants' Product.

177. The FDA-approved label of Defendants' Product provides that "Ephedrine sulfate injection, 25mg/5ml (5 mg/mL) in a pre-filled syringe, is a premixed formulation. Do not dilute prior to use." Exhibit D at Dosage and Administration, section 2.1.

178. On information and belief, Hikma has no reasonable basis for believing that Hikma will not induce direct infringement of one or more claims of the '398 patent and no reasonable basis for believing that the infringed claims are invalid.

179. Hikma's manufacture, use, importation, sale, or offer for sale of Defendants' Product constitutes willful infringement.

180. This case is "exceptional," and Nexus is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

181. The acts of infringement by Hikma set forth above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

182. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, importing, offering for sale, or selling Defendants' Product in the United States before expiration of the '398 patent.

COUNT VII
DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '398 PATENT

183. Nexus incorporates and realleges the foregoing paragraphs.

184. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. §§ 100 et seq., including 35 U.S.C. § 271(b) and/or (c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

185. To the extent that Hikma contends that there has been no manufacture, use, sale, importation or offer for sale of Defendants' Product at this time, there is still an actual case or controversy such that the Court may entertain Nexus's request for declaratory relief consistent with Article III of the United States Constitution, and that actual case or controversy requires a declaration of rights by this Court.

186. On information and belief, FDA's approval of Defendants' Product, coupled with Hikma's commercial activities in support of the imminent manufacture, importation and/or launch of Defendants' Product, including at least: (i) Hikma's application to the FDA for permission to market Defendants' Product; and (ii) and Hikma's commitment to commercializing Defendants' Product, create an actual, immediate, and real controversy under the Declaratory Judgment Act that

Hikma will actively induce and/or contribute to infringement of valid and enforceable claims of the '398 patent before the '398 patent's expiration in violation of 35 U.S.C. § 271(b) and/or (c).

187. On information and belief, Hikma has engaged in and will continue to engage in substantial activities in preparation to manufacture, market, sell and offer to sell Defendants' Product in the United States with an FDA-approved package insert that will direct healthcare providers and patients in the use of Defendants' Product.

188. A healthcare provider will directly infringe, either literally or under the doctrine of equivalents, one or more of the claims of the '398 patent. Specifically, on information and belief, a healthcare provider administering Defendants' Product in accordance with the Defendants' Product package insert, will perform all of the steps of one or more claims of the '398 patent.

189. On information and belief, Hikma, currently does and/or previously did, actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hikma knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent by marketing Defendants' Product with the FDA-approved package insert. Specifically, a healthcare provider administering Defendants' Product in accordance with Hikma's package insert will perform all of the steps of one or more claims of the '398 patent.

190. On information and belief, Hikma has no reasonable basis for believing that Hikma will not induce direct infringement of one or more claims of the '398 patent and no reasonable basis for believing that the infringed claims are invalid.

191. Hikma's manufacture, use, importation, sale, or offer for sale of Defendants' Product constitutes willful infringement.

192. This case is "exceptional," and Nexus is entitled to an award of reasonable attorneys' fees under 35 U.S.C. § 285.

193. The acts of infringement by Hikma set forth above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

194. Nexus is entitled to an injunction prohibiting Hikma from manufacturing, using, importing, offering for sale, or selling Defendants' Product in the United States before expiration of the '398 patent.

COUNT VIII
INFRINGEMENT OF THE '398 PATENT UNDER § 271(e)(2)

195. Nexus incorporates and realleges the foregoing paragraphs.

196. Hikma's submission of ANDA No. 217721, and supplementations thereto, to the FDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act to obtain approval to manufacture, market, sell, and offer to sell Defendants' Product with an FDA approved package insert that has or will, on information and belief, direct healthcare providers and patients in the use of Defendants' Product in a way that is claimed in the '398 patent, constitutes an act of infringement under 35 U.S.C. § 271(e)(2).

197. On information and belief, Hikma has or will soon actively and intentionally aid, abet, encourage, participate, and induce others to perform acts that Hikma knows will directly infringe, either literally or under the doctrine of equivalents, one or more claims of the '398 patent by marketing Defendants' Product with the FDA-approved package insert, and these acts actively induce infringement and/or contribute to infringement of one or more claims of the '398 patent literally and/or under the doctrine of equivalents, under 35 U.S.C. § 271(b) and/or (c).

198. On information and belief, Hikma has engaged in and will continue to engage in substantial activities in preparation to manufacture, market, sell and offer to sell Defendants' Product in the United States with an FDA-approved package insert that will direct healthcare providers and patients in the use of Defendants' Product.

199. On information and belief, and based on publicly available information, a healthcare provider will directly infringe one of more of the claims of the '398 patent by administering Defendants' Product in accordance with Hikma's package insert.

200. On information and belief, the current and/or imminent manufacture, importation, use, sale, or offer for sale of Defendants' Product is covered by the claims of the '398 patent, and one or more of Hikma's actions constitutes induced infringement of the '398 patent.

201. On information and belief, unless enjoined by this Court, Hikma will infringe one or more claims of the '398 patent by actively inducing infringement and/or contributing to infringement by others under 35 U.S.C. § 271(b) and/or (c).

202. On information and belief, Hikma has no reasonable basis for believing that Hikma will not induce direct infringement of one or more claims of the '398 patent and no reasonable basis for believing that the infringed claims are invalid.

203. This case is "exceptional," as that term is used in 35 U.S.C. § 285.

204. The acts of infringement by Hikma above will cause Nexus irreparable harm for which it has no adequate remedy at law, and those acts will continue unless enjoined by this Court.

205. Nexus is entitled to the relief provided by 35 U.S.C. § 271(e)(4)(A), (B), and/or (C) including statutory relief, injunctive relief, and/or damages.

PRAYER FOR RELIEF

WHEREFORE, Nexus respectfully requests the following relief:

A. A judgment, pursuant to 35 U.S.C. § 271(e)(2) and 35 U.S.C. § 271(a), (b), (c), and/or (g), that the commercial manufacture, use, offering to sell, or sale within the United States, and/or importation into the United States, of Defendants' Product on or after October 11, 2022, and before the expiration of the '752 patent (including any regulatory extension), has infringed the '752 patent;

B. A judgment, pursuant to 35 U.S.C. § 271(a), (b), (c), and/or (g), that the commercial manufacture, use, offering to sell, or sale within the United States, and/or importation into the United States, of Defendants' Product on or after August 30, 2022, and before the expiration of the '369 patent (including any regulatory extension), has infringed the '369 patent;

C. A judgment, pursuant to 35 U.S.C. § 271(e)(2) and 35 U.S.C. § 271(b) and/or (c), that the commercial manufacture, use, offering to sell, or sale within the United States, and/or importation into the United States, of Defendants' Product on or after February 7, 2023, and before the expiration of the '398 patent (including any regulatory extension), has infringed the '398 patent;

D. A declaration, pursuant to 28 U.S.C. §§ 2201 and 2202, that the commercial manufacture, use, offering to sell, or sale within the United States, and/or importation into the United States, of Defendants' Product will infringe the '752 and '369 patents under 35 U.S.C. § 271(a), (b), (c), and/or (g);

E. A declaration, pursuant to 28 U.S.C. §§ 2201 and 2202, that the commercial manufacture, use, offering to sell, or sale within the United States, and/or importation into the

United States, of Defendants' Product will induce or contribute to infringement of the '398 patent under 35 U.S.C. § 271(b) or (c);

F. A judgment, pursuant to 35 U.S.C. § 271(e)(4)(A) and other provisions of 35 U.S.C. § 271 that the effective date of the approval of Hikma's Application Number 217721 is not earlier than the expiration date of the '752 patent, '369 patent, and '398 patent plus any additional period of exclusivity.

G. A judgment, pursuant to 35 U.S.C. § 271(e)(4)(B) and other provisions of 35 U.S.C. § 271, that Hikma is prevented from manufacturing, using, importing, selling, or offering to sell Defendants' Product until a date not earlier than the date of expiration of the '752 patent, '369 patent, and '398 patent plus any additional period of exclusivity;

H. A judgment that the Patents-In-Suit are valid and enforceable;

I. An order for preliminary and permanent injunction for Hikma's unlawful conduct;

J. An award, pursuant to 35 U.S.C. § 271(e)(4)(C) and/or 35 U.S.C. § 284, of damages or other monetary relief to compensate Nexus for Hikma's engagement in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of Defendants' Product, or any product the making, using, offering for sale, sale, marketing, distribution, and/or importation of which infringes the Patents-In-Suit;

K. Awarding Nexus enhanced damages;

L. A judgment pursuant to 35 U.S.C. § 285 that this case against Hikma is an exceptional case and an award of attorneys' fees and costs; and

M. Such other and further relief to Nexus as this Court may deem just and proper.

DEMAND FOR A JURY TRIAL

Nexus hereby demands a jury trial on all issues so triable.

/s/ Kelly E. Farnan
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