IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BAXALTA INCORPORATED, BAXALTA US INC., and NEKTAR THERAPEUTICS,	
Plaintiffs,	C.A. No. _____
v.	**JURY TRIAL DEMANDED**
BAYER HEALTHCARE LLC,	
Defendant.	

COMPLAINT FOR PATENT INFRINGEMENT

Baxalta Incorporated ("Baxalta Inc.") and Baxalta US Inc. ("Baxalta US") (collectively, "Baxalta"), and Nektar Therapeutics ("Nektar") (collectively, "Plaintiffs"), by their attorneys, allege as follows for their Complaint for Patent Infringement against Bayer HealthCare LLC ("Bayer" or "Defendant"):

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the patent laws of United States, Title 35, United States Code and Title 28, United States Code concerning U.S. Patent No. 7,199,223 (Ex. A, "the '223 patent"); U.S. Patent No. 7,863,421 (Ex. B, "the '421 patent"); U.S. Patent No. 8,143,378 (Ex. C, "the '378 patent"); U.S. Patent No. 8,247,536 (Ex. D, "the '536 patent"); U.S. Patent No. 8,519,102 (Ex. E, "the '102 patent"); U.S. Patent No. 8,618,259 (Ex. F, "the '259 patent"); and U.S. Patent No. 8,889,831 (Ex. G, "the '831 patent").

2. This action is related to the following case pending in the District of Delaware filed by Bayer: *Bayer HealthCare LLC v. Baxalta Inc., et al.*, No. 16-1122-RGA (D. Del.) ("the First Delaware Action").

3. This action and the First Delaware Action are related actions. They both involve the same or substantially the same subject matter, facts, and witnesses. Both actions concern poly(ethylene glycol) ("PEG") bound to Factor VIII ("FVIII-PEG").

THE PARTIES

4. Plaintiff Baxalta Inc. is a corporation organized under the laws of Delaware with its principal place of business at 1200 Lakeside Drive, Bannockburn, Illinois, 60015.

5. Plaintiff Baxalta US is a corporation organized under the laws of Delaware, having its principal place of business at 1200 Lakeside Drive, Bannockburn, Illinois, 60015.

6. Plaintiff Nektar is a corporation organized under the laws of Delaware with its principal place of business at 455 Mission Bay Boulevard South, San Francisco, California, 94158.

7. Upon information and belief, Bayer is a corporation organized under the laws of Delaware with its principal place of business at 100 Bayer Boulevard, Whippany, New Jersey, 07891.

JURISDICTION AND VENUE

8. This civil action for patent infringement arises under the patent laws of the United States, 35 U.S.C. §§ 1 *et seq.* and 28 U.S.C. §§ 2201 *et seq.*

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

10. This Court has personal jurisdiction over Defendant because, *inter alia*, it resides in Delaware, it is doing business in Delaware, and it has continuous and systematic contacts with this Judicial District. Upon information and belief, Defendant derives substantial revenue from articles marketed, sold, distributed, and/or used in this Judicial District. Upon information and belief, Defendant maintains a registered agent for service of process in this Judicial

District. Upon information and belief, Defendant has submitted to jurisdiction in this Judicial District without contesting personal jurisdiction. *See, e.g.*, *Roche Diagnostics Operations, Inc. v. Abbott Diabetes Care, Inc.*, No. 07-cv-00753 (D. Del. Jan. 11, 2008), D.I. 41. Furthermore, Defendant has availed itself of the rights, benefits, and privileges of this Judicial District by seeking affirmative relief from this Judicial District in a litigation that is currently pending in this Judicial District. *See, e.g.*, Ex. H, Complaint, *Bayer HealthCare LLC v. Baxalta Inc., et al.*, No. 16-cv-1122-RGA (D. Del. Dec. 5, 2016), D.I. 1.

11. Venue is proper in this Judicial District pursuant to 28 U.S.C. §§ 1391(b) and (c), and § 1400(b).

FACTS AS TO ALL COUNTS

12. Plaintiffs and Defendant are currently parties to proceedings in the United States and Germany adjudicating claims of infringement, validity, and ownership, each of which involve the same or substantially the same subject matter, facts, and witnesses. Both actions concern FVIII-PEG.

13. Plaintiff Nektar and Defendant Bayer entered into a Research Agreement in December 2003 ("the Research Agreement").

14. Pursuant to the Research Agreement, Nektar and Bayer conducted research relating to FVIII-PEG.

15. Pursuant to the Research Agreement, Nektar employees communicated Nektar proprietary information in the period from 2003 to 2004 concerning, *inter alia*, Nektar's Core Technology that was subject to the confidentiality provisions under the Research Agreement to at least Bayer employee Dr. Clark Q. Pan.

16. Nektar employees provided Dr. Pan with samples of FVIII-PEG, as well as reports corresponding to the work performed.

17. The samples Nektar sent to Dr. Pan included a B-domain deleted ("BDD") Factor VIII polypeptide bound to PEG.

18. Bayer did not renew the Research Agreement.

19. Upon information and belief, in November 2004, Bayer proceeded to prosecute a series of patent applications ("the Bayer FVIII-PEG patent family") in at least the United States and in Europe directed to Nektar's Core Technology in violation of the Research Agreement.

20. Nektar did not consent to or authorize Bayer to file or prosecute to issuance the Bayer FVIII-PEG patent family.

21. The Bayer FVIII-PEG patent family includes U.S. Patent No. 9,364,520; EP 2 371 856; and EP 2 363 414; among others. Upon information and belief, U.S. Patent No. 9,364,520; EP 2 371 856; and EP 2 363 414 list, on their faces, Clark Q. Pan, John E. Murphy, Baisong Mei, Jonathan S. Strauss, Hendri Tjandra, Jianmin Chen, Thomas Barnett, Liang Tang, and Deqian Wang as the named inventors.

22. Before, during, and after the Research Agreement, Nektar filed patent applications directed to, *inter alia*, the Nektar Core Technology in the United States and abroad. These patent applications ultimately issued as the '223 patent; the '421 patent; the '378 patent; the '536 patent; the '102 patent; the '259 patent; the '831 patent; and also resulted in the following European patent filings: EP 1 596 887; EP 2 338 523; EP 2 572 732; and EP 2 572 733.

23. There are at least two pending proceedings between Nektar and Bayer concerning FVIII-PEG technology in Germany ("the European Proceedings").

24. On September 30, 2013, Bayer filed patent vindication proceedings against Nektar Therapeutics AL, Corporation in the District Court in Munich, Germany, seeking

ownership rights to certain Nektar patent filings, including EP 1 596 887; EP 2 338 523; EP 2 572 732; and EP 2 572 733.

25. On November 18, 2015, Nektar filed a patent vindication proceeding against Bayer in Germany, seeking ownership rights to certain Bayer patent filings directed to Nektar's Core Technology, including EP 2 371 856 and EP 2 363 414, based, in part, on Bayer's violation of the terms of the Research Agreement when it pursued these patent filings.

26. On December 5, 2016, Bayer filed an action in this Judicial District against Baxalta Inc., Baxalta US, and Nektar for the alleged infringement of U.S. Patent No. 9,364,520 ("the '520 patent"), titled "Factor VIII Conjugates." *See* Ex. H.

27. The '520 patent issued from a patent application within the Bayer FVIII-PEG patent family. Bayer's pursuit of the claims within said patent application was in violation of the Research Agreement.

28. In addition to its infringement allegations, Bayer's Complaint in the First Delaware Action sets forth and relies on allegations concerning the treatment of hemophilia A with Factor VIII, Bayer's Factor VIII products, the Research Agreement, and the European Proceedings. *See* Ex. H at ¶¶ 14–17, 21, 30–40.

29. Bayer's Complaint in the First Delaware Action puts directly at issue what Nektar and Bayer did pursuant to the Research Agreement, as well as the arguments advanced in the European Proceedings. For instance, Bayer alleges, *inter alia*, that "Nektar provided certain samples of randomly pegylated recombinant human Factor VIII (full length and BDD variants) to Bayer as well as a report corresponding to the work performed," (*see* Ex. H at ¶ 32), "Bayer elected to not renew the Agreement and instead discontinued the relationship with Nektar upon conclusion of Nektar's work contemplated under the Agreement," (*Id.* at ¶ 34), and "Bayer, who

had previously commenced its own independent research into pegylation of Factor VIII, continued its research and development work, which eventually culminated in the '520 patent." *Id.* at ¶ 35.

30. Bayer further alleges in the First Delaware Action that "Nektar filed its own action against Bayer in 2015 in the courts of Munich, Germany, seeking rights to certain Bayer patent applications pending in the European Patent Office related to pegylation of Factor VIII," and that "Nektar relies, in part, on the Agreement in claiming that it is entitled to rights in these applications." *Id.* at ¶ 37.

31. In the First Delaware Action, Baxalta Inc., Baxalta US, and Nektar set forth invalidity, license, and ownership/standing defenses that involve subject matter, facts, and witnesses related to the ownership, research and development, and inventorship of the subject matter of the '520 patent. *See* Defendants Baxalta Inc. and Baxalta US Inc.'s Answer and Defenses to Plaintiff's Complaint, No. 1:16-cv-1122-RGA, D.I. 28 (Aug. 24, 2017) ("Baxalta Answer") (Ex. I); Defendant Nektar Therapeutics' Answer and Defenses to Plaintiff's Complaint, No. 1:16-cv-1122-RGA, D.I. 29 (Aug. 24, 2017) ("Nektar Answer") (Ex. J).

32. For example, Baxalta Inc., Baxalta US, and Nektar each asserted invalidity defenses directed to: (i) the improper derivation of the purported invention of the '520 patent by another under 35 U.S.C. § 102(f), and (ii) the prior conception and reduction-to-practice of the purported invention of the '520 patent by another under 35 U.S.C. § 102(g), which implicate efforts at Miles Laboratories ("Miles") (a predecessor company to Bayer) and development work at that company deemed as unsuccessful by Miles, as well as the work that Nektar and Bayer each conducted independently from, and pursuant to, the Research Agreement. *See* Ex. I at 11; Ex. J at 11–12. Further, as support for its ownership/standing defense, Nektar has alleged that it

is the owner of the ’520 patent “by virtue of the Research Agreement . . . and/or the collaboration between” Nektar and Bayer employees. Ex. J at 12.

33. On August 30, 2017, Bayer filed a Complaint in the Northern District of California, seeking a judgment of non-infringement and invalidity of U.S. Patent No. 7,858,749 (“the ’749 patent”) based on Bayer’s filing of Biologics License Application (“BLA”) No. 125661 (“the ’749 Patent Infringement Action”). *See* Complaint, *Bayer HealthCare LLC v. Nektar Therapeutics, et al.*, No. 5:17-cv-05055 (N.D. Cal. Aug. 30, 2017), D.I. 1 (“’749 Patent Infringement Complaint”) (Ex. K).

34. The First Delaware Action relies on the same or substantially the same subject matter, facts, and witnesses as the present action. Both the First Delaware Action and the present action concern FVIII-PEG technology.

I. THE PATENTS-IN-SUIT

35. On February 26, 2003, Nektar filed U.S. Provisional Application No. 60/450,578 (“the Nektar provisional application”).

A. U.S. Patent No. 7,199,223

36. The ’223 patent, titled “Polymer-Factor VIII Moiety Conjugates,” was duly and legally issued by the United States Patent and Trademark Office (“USPTO”) on April 3, 2007.

37. The ’223 patent claims priority to the Nektar provisional application.

38. Nektar is the owner by assignment of the ’223 patent. Nektar has granted Baxalta a license to the ’223 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’223 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’223 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

B. U.S. Patent No. 7,863,421

39. The ’421 patent, titled “Polymer-Factor VIII Moiety Conjugates,” was duly and legally issued by the USPTO on January 4, 2011.

40. The ’421 patent is a continuation of application No. 11/702,302, which later issued as the ’749 patent. The ’749 patent is a continuation of the ’223 patent. The ’421 patent contains a claim of priority to the Nektar provisional application.

41. Nektar is the owner by assignment of the ’421 patent. Nektar has granted Baxalta a license to the ’421 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’421 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’421 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

C. U.S. Patent No. 8,143,378

42. The ’378 patent, titled “Polymer Factor VIII Moiety Conjugates,” was duly and legally issued by the USPTO on March 27, 2012.

43. The ’378 patent is a continuation of the ’749 patent, which is a continuation of the ’223 patent. The ’378 patent contains a claim of priority to the Nektar provisional application.

44. Nektar is the owner by assignment of the ’378 patent. Nektar has granted Baxalta a license to the ’378 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’378 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’378 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

D. U.S. Patent No. 8,247,536

45. The ’536 patent, titled “Factor VIII Compositions,” was duly and legally issued by the USPTO on August 21, 2012.

46. The ’536 patent is a continuation of the ’749 patent, which is a continuation of the ’223 patent. The ’536 patent contains a claim of priority to the Nektar provisional application.

47. Nektar is the owner by assignment of the ’536 patent. Nektar has granted Baxalta a license to the ’536 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’536 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’536 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

E. U.S. Patent No. 8,519,102

48. The ’102 patent, titled “Polymer Factor VIII Moiety Conjugates,” was duly and legally issued by the USPTO on August 27, 2013.

49. The ’102 patent is a continuation of the ’536 patent, which is a continuation of the ’749 patent, which is a continuation of the ’223 patent. The ’102 patent contains a claim of priority to the Nektar provisional application.

50. Nektar is the owner by assignment of the ’102 patent. Nektar has granted Baxalta a license to the ’102 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’102 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’102 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

F. U.S. Patent No. 8,618,259

51. The ’259 patent, titled “Polymer-Factor VIII Conjugate Compositions,” was duly and legally issued by the USPTO on December 31, 2013.

52. The ’259 patent is a continuation of the ’536 patent, which is a continuation of the ’749 patent, which is a continuation of the ’223 patent. The ’259 patent contains a claim of priority to the Nektar provisional application.

53. Nektar is the owner by assignment of the ’259 patent. Nektar has granted Baxalta a license to the ’259 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’259 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’259 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

G. U.S. Patent No. 8,889,831

54. The ’831 patent, titled “Unit Dosage Forms of Pharmaceutical Compositions Comprising a Polymer-Factor VIII Polypeptide Conjugate,” was duly and legally issued by the USPTO on November 18, 2014.

55. The ’831 patent is a continuation of the ’536 patent, which is a continuation of the ’749 patent, which is a continuation of the ’223 patent. The ’831 patent contains a claim of priority to the Nektar provisional application.

56. Nektar is the owner by assignment of the ’831 patent. Nektar has granted Baxalta a license to the ’831 patent, whereby Baxalta has the right to make, use, offer for sale, or sell products that would otherwise infringe the ’831 patent in the United States. Pursuant to this license, Baxalta has the right to assert against third parties all causes of action arising under the ’831 patent, and Nektar and Baxalta have the right to any remedies for infringement thereof.

II. Hemophilia

57. Hemophilia A is a congenital bleeding disorder caused by deficient or defective coagulation, which requires the interaction of platelets and blood coagulation factors to coagulate or clot the blood. Patients suffering from hemophilia A are afflicted with a deficiency in the

activity and/or amount of Factor VIII protein, which is a key protein in the blood coagulation pathway and is, therefore, critical for proper blood coagulation and the control of bleeding. Hemophilia A patients can experience a range of serious consequences, such as hemorrhages in the joints and muscles as well as bleeding in the digestive system and brain. Without the constant presence of functional Factor VIII in the body, hemophilia A patients can suffer severe and even fatal bleeding episodes. Hemophilia A presently affects approximately 400 newborn babies in the United States annually and over 400,000 people worldwide.

58. Baxalta is one of the world's leading providers of products used in the treatment of hemophilia. Baxalta's products include ADVATE® [Antihemophilic Factor (Recombinant)] and ADYNOVATE® [Antihemophilic Factor (Recombinant), PEGylated].

59. Baxalta US owns BLA No. 125566, which was approved by the FDA on November 13, 2015 for the manufacture and sale of ADYNOVATE®. ADYNOVATE® is "a human antihemophilic factor indicated in children and adults with hemophilia A (congenital factor VIII deficiency) for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes." Ex. L.

III. Defendant's Infringing Product

60. Defendant has made representations to a United States Federal District Court regarding the character of the BAY 94-9027 ("BAY 94") product, the regulatory status of the BAY 94 product, and its preparedness to commercialize the BAY 94 product. *See* Ex. K at ¶¶ 65–71, 81, 92–93.

61. Upon information and belief, Defendant filed BLA No. 125661 for BAY 94 with the FDA on August 30, 2017, seeking approval for the treatment of hemophilia A. Ex. K at ¶ 66.

62. Upon information and belief, the active ingredient in BAY 94 is the recombinant BDD form of Factor VIII pegylated with a 60kDa PEG molecule. Upon information and belief,

the BAY 94 manufacturing process entails, *inter alia*, introduction of a cysteine and pegylation of a BDD Factor VIII with a 60 kDa PEG molecule attached via a thioether linkage to the introduced cysteine. Ex. K at ¶ 69.

63. Upon information and belief, BAY 94 is intended to be administered intravenously and will be available as a lyophilized powder containing 250, 500, 1000, 2000, or 3000 International Units ("IU"). Upon information and belief, BAY 94 is produced without the addition of any exogenous human or animal derived protein in the cell culture process, purification, pegylation, or final formulation. Ex. K at ¶ 70.

64. There is a substantial controversy between Defendant and Plaintiffs, whose legal interests are adverse. The controversy is of sufficient immediacy and reality to warrant the issuance of a judgment. Ex. K at ¶ 81.

65. Bayer asserts that there is a substantial controversy between Bayer and Plaintiffs, whose legal interests are adverse. Bayer further asserts that the controversy is of sufficient immediacy and reality to warrant the issuance of a judgment. *Id.*

66. Upon information and belief, Bayer has made meaningful preparations to manufacture, use, offer to sell, and/or sell its BAY 94 product in the United States. Ex. K at ¶ 81.

67. Upon information and belief, Bayer has hired and continues to grow its sales force in order to promote the marketing and sale of BAY 94 in the United States upon FDA approval, including by hiring additional sales people. For example, upon information and belief, Bayer has posted publicly available job postings for the position of Director of Sales Hematology as recently as August 16, 2017. Upon further information and belief, Bayer's sales force will begin actively marketing BAY 94 immediately upon receiving FDA approval. Ex. K at ¶ 89.

68. Upon information and belief, Bayer has a manufacturing facility for the commercial manufacture of BAY 94 to accommodate the demand for BAY 94 following FDA approval. Upon information and belief, Bayer has the capability to manufacture BAY 94 upon FDA approval. Ex. K at ¶ 91.

69. Upon information and belief, according to standard industry practice, the FDA typically takes about one year to complete its review of a BLA. Upon information and belief, FDA approval of BAY 94 would permit Bayer to immediately offer to sell and sell the treatment within the United States. Upon information and belief, Bayer expects to launch BAY 94 in the United States in the fourth quarter of 2018. Ex. K at ¶ 92.

70. Upon information and belief, following the approval of Bayer's BLA, BAY 94 will be indicated for an overlapping patient population as ADYNOVATE® and will, therefore, compete with Baxalta's ADYNOVATE® product. Ex. K at ¶ 93.

71. In sum, upon information and belief, Bayer has made meaningful preparations to manufacture, use, offer to sell, and/or sell its BAY 94 product in the United States, including in this Judicial District. Upon information and belief, Bayer has submitted a BLA seeking FDA approval to commercially market its BAY 94 product, which Bayer expects to be approved in the fourth quarter of 2018. Bayer's infringing acts as described herein will immediately and irreparably harm Plaintiffs.

72. As a direct and proximate result of Bayer's acts of infringement, Plaintiffs will suffer damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

FIRST COUNT
(Infringement of the ’223 patent by Bayer)

73. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

74. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

75. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

76. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the ’223 patent.

77. Claim 1 of the ’223 patent recites:

> A conjugate comprising one, two or three water-soluble polymers covalently attached to a Factor VIII moiety, wherein each water-soluble polymer has a nominal average molecular weight in the range of from 6,000 Daltons to 150,000 Daltons and further wherein the cojugate [sic] is a 1-mer, 2-mer or 3-mer.

78. BAY 94 satisfies the claim limitation “one, two, or three water-soluble polymers covalently attached to a Factor VIII moiety.” Upon information and belief, BAY 94 is comprised of Factor VIII polypeptide conjugated with PEG. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a “recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII”); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is “pegylated with a large 60 kDa PEG molecule”). PEG is a water-soluble polymer (*see* ’223 patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. N at 270 (“PEGylation is the covalent attachment of long-

chained chemically activated polyethylene glycol (PEG) molecules to proteins."). Upon information and belief, there is a water-soluble polymer attached to the Factor VIII moiety that is in BAY 94. Ex. M at 82 (showing a PEG conjugated to the Factor VIII moiety at amino acid position 1804).

79. BAY 94 satisfies the claim limitation "wherein each water-soluble polymer has a nominal average molecular weight in the range of from 6,000 Daltons to 150,000 Daltons." Upon information and belief, BAY 94 is comprised of a conjugate that is pegylated with a 60 kDa water-soluble polymer. Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is a "recombinant [B-domain deleted] form of Factor VIII pegylated with a large 60 kDa PEG molecule."). Ex. N at 271–72.

80. BAY 94 satisfies the claim limitation "and further wherein the cojugate [sic] is a 1-mer, 2-mer or 3-mer." Upon information and belief, BAY 94 comprises a conjugate that is pegylated at an amino acid position with a water-soluble polymer. Ex. M at 82 (showing a PEG conjugated to the Factor VIII moiety at amino acid position 1804).

81. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '223 patent. Plaintiffs have no adequate remedy at law.

82. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

83. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

SECOND COUNT
(Infringement of the ’421 patent by Bayer)

84. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

85. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

86. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

87. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the ’421 patent.

88. Claim 1 of the ’421 patent recites:

> A conjugate comprising a water-soluble polymer covalently attached to a Factor VIII polypeptide via a thiol group of a cysteine residue contained within the Factor VIII polypeptide, wherein the Factor VIII polypeptide is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII, and wherein the water-soluble polymer is selected from the group consisting of poly(alkylene glycol), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, and poly(N-acryloylmorpholine.

89. BAY 94 satisfies the claim limitation “a water-soluble polymer covalently attached to a Factor VIII polypeptide.” Upon information and belief, BAY 94 is comprised of Factor VIII polypeptide conjugated with PEG. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a “recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII”); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is “pegylated with a large 60 kDa PEG molecule”). PEG is a water-soluble polymer (*see* ’223

patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

90. BAY 94 satisfies the claim limitation "via a thiol group of a cysteine residue contained within the Factor VIII polypeptide." Upon information and belief, BAY 94 is comprised of a conjugate wherein the PEG is bound via a thiol group at a cysteine residue located within the Factor VIII polypeptide. Ex. K at ¶ 69 ("PEG molecule [is] attached via a thioether linkage to the introduced cysteine."); Ex. N at 271; Ex. M at 82.

91. BAY 94 satisfies the claim limitation "wherein the Factor VIII polypeptide is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII." Upon information and belief, BAY 94 is comprised of a B-domain deleted Factor VIII polypeptide. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII").

92. BAY 94 satisfies the claim limitation "and wherein the water-soluble polymer is selected from the group consisting of poly(alkylene glycol), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, and poly(N-acryloylmorpholine)." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

93. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '421 patent. Plaintiffs have no adequate remedy at law.

94. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

95. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

THIRD COUNT

(Infringement of the '378 patent by Bayer)

96. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

97. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

98. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

99. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '378 patent.

100. Claim 1 of the '378 patent recites:

> A composition comprising a plurality of conjugates, each conjugate comprising one, two or three water-soluble polymers each covalently attached to a Factor VIII moiety polypeptide via a hydrolytically stable linkage, wherein: (i) the Factor VIII polypeptide is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII; (ii) the water-

> soluble polymer is selected from the group consisting of a poly(alkylene glycol), a poly(oxyethylated polyol), a poly (olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxy-alkylmethacrylamide), a poly(hydroxyalkylmethacrylate), a poly(saccharide), a poly(α-hydroxy acid), a poly(vinyl alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof; and (iii) the composition is bioactive, comprising an in-vitro activity of at least 15% compared to that of a Factor VIII polypeptide composition in unconjugated form.

101. BAY 94 satisfies the claim limitation "a plurality of conjugates, each conjugate comprising one, two or three water-soluble polymers each covalently attached to a Factor VIII moiety polypeptide." Upon information and belief, BAY 94 is comprised of Factor VIII polypeptide conjugated with PEG. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII"); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"). There are 19 cysteines in a BDD Factor VIII. Ex. N at 271. PEG is a water-soluble polymer (*see* '223 patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins."). Upon information and belief, a water-soluble polymer attached to the Factor VIII moiety in the BAY 94 product. Ex. M at 82 (showing a PEG conjugated to the Factor VIII moiety at amino acid position 1804).

102. BAY 94 satisfies the claim limitation "via a hydrolytically stable linkage." Bayer characterizes its product as comprising a conjugate that is pegylated via a thioether linkage. Ex. K at ¶ 111 ("BAY 94 is pegylated via a thioether linkage to a cysteine residue."). Ex. N at 271; Ex. M at 82. Bayer further characterizes a thioether linkage as a "hydrolytically stable linkage." Ex. K at ¶ 111.

103. BAY 94 satisfies the claim limitation "wherein: (i) the Factor VIII polypeptide is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII." Upon information and belief, BAY 94 is comprised of a B-domain deleted Factor VIII polypeptide. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII").

104. BAY 94 satisfies the claim limitation "(ii) the water-soluble polymer is selected from the group consisting of a poly(alkylene glycol), a poly(oxyethylated polyol), a poly(olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxyalkylmethacrylamide), a poly(hydroxyalkylmethacrylate), a poly(saccharide), a poly(α-hydroxy acid), a poly(vinyl alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

105. BAY 94 satisfies the claim limitation "and (iii) the composition is bioactive, comprising an in-vitro activity of at least 15% compared to that of a Factor VIII polypeptide composition in unconjugated form." Upon information and belief, BAY 94 comprises a conjugate that retains activity compared to an unconjugated Factor VIII polypeptide. Ex. N at 273–74 ("K1804C . . . exhibited no effect on FVIII activity by the addition of PEG up to 60 kDa . . . . The specific activity, as measured by the 2-stage chromogenic assay of [this] 60-kDa PEG-FVIII variant[] after cation exchange chromatography, was similar to that before PEGylation.

Full retention of activity was also seen when the 1-stage activated partial thromboplastin time assay was used.").

106. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '378 patent. Plaintiffs have no adequate remedy at law.

107. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

108. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

FOURTH COUNT
(Infringement of the '536 patent by Bayer)

109. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

110. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

111. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94 or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

112. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '536 patent.

113. Claim 1 of the '536 patent recites:

> A composition that is free from albumin comprising:
>
> a conjugate that comprises one, two or three water-soluble

> polymers selected from the group consisting of a poly (alkylene glycol), a poly(oxyethylated polyol), a poly (olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxyalkylmethacrylamide), a poly (hydroxyalkylmethacrylate), a poly(saccharide), a poly (α-hydroxy acid), a poly(vinyl alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof, covalently attached to a Factor VIII polypeptide selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII.

114. BAY 94 satisfies the claim limitation "a conjugate that comprises one, two or three water-soluble polymers." Upon information and belief, BAY 94 is comprised of a Factor VIII polypeptide conjugated with PEG. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII"); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"). PEG is a water-soluble polymer. *See* the '223 patent, col.3 ll.56–58. Upon information and belief, there is a water-soluble polymer attached to the Factor VIII moiety in the BAY 94 product. Ex. M at 82 (showing a PEG conjugated to the Factor VIII moiety at amino acid position 1804).

115. BAY 94 satisfies the claim limitation "selected from the group consisting of poly(alkylene glycol), a poly(oxyethylated polyol), a poly(olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxyalkylmethacrylamide), a poly(hydroxyalkylmethacrylate), a poly(saccharide), a poly(α-hydroxy acid), a poly(vinyl alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG

molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

116. BAY 94 satisfies the claim limitation "covalently attached to a Factor VIII polypeptide selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF and B-domain deleted Factor VIII." Upon information and belief, BAY 94 is comprised of a B-domain deleted Factor VIII polypeptide. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII").

117. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '536 patent. Plaintiffs have no adequate remedy at law.

118. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

119. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

FIFTH COUNT
(Infringement of the '102 patent by Bayer)

120. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

121. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

122. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

123. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the ’102 patent.

124. Claim 1 of the ’102 patent recites:

> A conjugate comprising a water-soluble polymer covalently attached to a Factor VIII polypeptide via a thiol group of a cysteine residue that has been added to or substituted in the Factor VIII polypeptide,
>
> wherein the conjugate comprises an in-vitro activity that is at least 15% of the in-vitro activity of the unconjugated Factor VIII polypeptide,
>
> and wherein the water-soluble polymer is selected from the group consisting of a poly (alkylene glycol), a poly(oxyethylated polyol), a poly (olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxyalkylmethacrylamide), a poly (hydroxyalkylmethacrylate), a poly(saccharide), a poly (α-hydroxy acid), a poly(vinyl alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof.

125. BAY 94 satisfies the claim limitation “a water-soluble polymer covalently attached to a Factor VIII polypeptide.” Upon information and belief, BAY 94 is comprised of Factor VIII polypeptide conjugated with a water-soluble polymer (PEG). Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a “recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII”); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is “pegylated with a large 60 kDa PEG molecule”). PEG is a water-soluble polymer (*see* the ’223 patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. N at 270 (“PEGylation is the

covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

126. BAY 94 satisfies the claim limitation "via a thiol group of a cysteine residue that has been added or substituted in the Factor VIII polypeptide." Upon information and belief, BAY 94 is comprised of a conjugate wherein the PEG is bound via a thiol group at a cysteine residue located in the Factor VIII polypeptide. Ex. K at ¶ 69 ("PEG molecule [is] attached via a thioether linkage to the introduced cysteine."); Ex. N at 271; Ex. M at 82. Upon further information and belief, BAY 94 is comprised of a conjugate wherein a cysteine that has been added or substituted into the Factor VIII polypeptide. Ex. K at ¶ 69 ("The BAY 94 manufacturing process entails, *inter alia*, introduction of a cysteine and pegylation of a BDD Factor VIII protein."); Ex. N at 271.

127. BAY 94 satisfies the claim limitation "wherein the conjugate comprises an in-vitro activity that is at least 15% of the in-vitro activity of the unconjugated Factor VIII polypeptide." Upon information and belief, BAY 94 comprises a conjugate that retains activity compared to an unconjugated Factor VIII polypeptide. Ex. N at 273–74 ("K1804C . . . exhibited no effect on FVIII activity by the addition of PEG up to 60 kDa . . . . The specific activity, as measured by the 2-stage chromogenic assay of [this] 60-kDa PEG-FVIII variant[] after cation exchange chromatography, was similar to that before PEGylation. Full retention of activity was also seen when the 1-stage activated partial thromboplastin time assay was used.").

128. BAY 94 satisfies the claim limitation "and wherein the water-soluble polymer is selected from the group consisting of poly(alkylene glycol), a poly(oxyethylated polyol), a poly(olefinic alcohol), a poly(vinylpyrrolidone), a poly(hydroxyalkylmethacrylamide), a poly(hydroxyalkylmethacrylate), a poly(saccharide), a poly(α-hydroxy acid), a poly(vinyl

alcohol), a polyphosphazene, a polyoxazoline, a poly(N-acryloylmorpholine), and combinations thereof." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

129. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '102 patent. Plaintiffs have no adequate remedy at law.

130. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

131. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

SIXTH COUNT

(Infringement of the '259 patent by Bayer)

132. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

133. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

134. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

135. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '259 patent.

136. Claim 1 of the ’259 patent recites:

> A composition that is at least 85% free from albumin, the composition comprising a conjugate comprising a water-soluble polymer covalently attached to a Factor VIII polypeptide via a thiol group of a cysteine residue that has been added to or substituted in the Factor VIII polypeptide, wherein the water-soluble polymer is selected from the group consisting of poly(alkylene glycol), poly(oxyethylated polyol), poly (olefinic alcohol), poly(vinylpyrrolidone), poly(hydroxyl-alkylmethacrylamide), poly (hydroxyalkylmethacrylate), poly(saccharide), poly(α-hydroxy acid), poly(vinyl alcohol), polyphosphazene, polyoxazoline, poly(N-acryloylmorpholine), and combinations thereof.

137. BAY 94 satisfies the claim limitation “a conjugate comprising a water-soluble polymer covalently attached to a Factor VIII polypeptide.” BAY 94 is comprised of Factor VIII polypeptide conjugated with a water-soluble polymer (PEG). Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a “recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII”); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is “pegylated with a large 60 kDa PEG molecule”). PEG is a water-soluble polymer (*see* ’223 patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a “recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII”); Ex. N at 270 (“PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.”).

138. BAY 94 satisfies the claim limitation “via a thiol group of a cysteine residue that has been added to or substituted in the Factor VIII polypeptide.” Upon information and belief, BAY 94 is comprised of a conjugate wherein the PEG is bound via a thiol group at a cysteine residue located within the Factor VIII polypeptide. Ex. K at ¶ 69 (“PEG molecule [is] attached via a thioether linkage to the introduced cysteine.”); Ex. N at 271; Ex. M at 82. Upon further

information and belief, BAY 94 is comprised of a conjugate wherein a cysteine that has been added or substituted into the Factor VIII polypeptide. Ex. K at ¶ 69 ("The BAY 94 manufacturing process entails, *inter alia*, introduction of a cysteine and pegylation of a BDD Factor VIII protein."); Ex. N at 271.

139. BAY 94 satisfies the claim limitation "wherein the water soluble polymer is selected from the group consisting of poly(alkylene glycol), poly(oxyethylated polyol), poly(olefinic alcohol), poly(vinylpyrrolidone), poly(hydroxylalkylmethacrylamide), poly (hydroxyalkylmethacrylate), poly(saccharide), poly(α-hydroxy acid), poly(vinyl alcohol), polyphosphazene, polyoxazoline, poly(N-acryloylmorpholine), and combinations thereof." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

140. Upon information and belief, BAY 94 is at least 85% free from albumin because it is produced without the addition of any exogenous human or animal derived protein in the cell culture process, purification, pegylation, or final formulation. Ex. K at ¶ 70; *See generally*, Ex. O.

141. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '259 patent. Plaintiffs have no adequate remedy at law.

142. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

143. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

SEVENTH COUNT
(Infringement of the '831 patent by Bayer)

144. Plaintiffs repeat and reallege each of the foregoing paragraphs as if fully set forth herein.

145. Upon information and belief, Bayer seeks FDA approval for the manufacture, marketing, sale, and/or distribution of BAY 94.

146. Upon information and belief, Bayer has manufactured, sold, offered for sale, and/or imported BAY 94, or has made meaningful preparations to manufacture, sell, offer for sale, and/or import BAY 94 upon, or in anticipation of, FDA approval.

147. BAY 94 and/or its manufacture satisfies each claim element of and infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '831 patent.

148. Claim 1 of the '831 patent recites:

> A unit dose of a pharmaceutical composition, the pharmaceutical composition comprising:
> (i) a conjugate comprising one, two or three water-soluble polymers, each covalently attached to a Factor VIII polypeptide via a thiol group of a cysteine residue that has been added to or substituted in the Factor VIII polypeptide, and
> (ii) a pharmaceutically acceptable excipient,
> wherein the Factor VIII polypeptide is present in the unit dose in an amount ranging from 0.001 mg to 100 mg, and further wherein the one, two or three water soluble polymers are selected from the group consisting of poly (alkylene glycol), poly(oxyethylated polyol), poly(olefinic alcohol), poly(vinylpyrrolidone), poly (hydroxylalkylmethacrylamide), poly (hydroxyalkylmethacrylate), poly(saccharide), poly(a-hydroxy acid), poly(vinyl alcohol), polyphosphazene, polyoxazoline, poly(N-acryloylmorpholine), and combinations of any of the foregoing.

149. BAY 94 satisfies the claim limitation "a conjugate comprising one, two or three water-soluble polymers, each covalently attached to a Factor VIII polypeptide." Upon information and belief, BAY 94 is comprised of Factor VIII polypeptide conjugated with PEG. Ex. M at 82 (describing BAY 94 as comprising a conjugate that is a "recombinant DNA derived pegylated B domain deleted human blood coagulation factor VIII"); Ex. K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"). PEG is a water-soluble polymer (*see* '223 patent, col.3 ll.56–58) and, upon information and belief, is covalently attached to Factor VIII in the BAY 94 product. Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins."). Upon information and belief, there is a water-soluble polymer attached to the Factor VIII moiety. Ex. M at 82 (showing a PEG conjugated to the Factor VIII moiety at amino acid position 1804 in the BAY 94 product).

150. BAY 94 satisfies the claim limitation "via a thiol group of a cysteine residue that has been added to or substituted in the Factor VIII polypeptide." Upon information and belief, BAY 94 is comprised of a conjugate wherein the PEG is bound via a thiol group at a cysteine residue located within the Factor VIII polypeptide. Ex. K at ¶ 69 ("PEG molecule [is] attached via a thioether linkage to the introduced cysteine."); Ex. N at 271; Ex. M at 82. Upon further information and belief, BAY 94 is comprised of a conjugate wherein a cysteine that has been added or substituted into the Factor VIII polypeptide. Ex. K at ¶ 69 ("The BAY 94 manufacturing process entails, *inter alia*, introduction of a cysteine and pegylation of a BDD Factor VIII protein."); Ex. N at 271.

151. BAY 94 satisfies the claim limitation "and (ii) a pharmaceutically acceptable excipient, wherein the Factor VIII polypeptide is present in the unit dose in an amount ranging

from 0.001 mg to 100 mg." Upon information and belief, BAY 94 will be available as a lyophilized powder containing 250, 500, 1000, 2000, or 3000 International Units. Ex. K at ¶ 70. Upon information and belief, the weight of the Factor VIII polypeptide in the BAY 94 product is approximately 167 kDa. Ex. N at 273 ("MALDI-MS analysis of FVIII [] before PEG conjugation detected A1 (46 kDa), A2 (43 kDa), and A3C1C2 (78 kDa) fragments."). The concentration of FVIII in plasma is approximately 1 nM. Ex. P at 37685. Thus, upon information and belief, BAY 94 will be available in an amount from 0.001 mg to 100 mg.

152. BAY 94 satisfies the claim limitation "and further wherein the one, two or three water soluble polymers are selected from the group consisting of poly(alkylene glycol), poly(oxyethylated polyol), poly(olefinic alcohol), poly(vinylpyrrolidone), poly(hydroxylalkylmethacrylamide), poly (hydroxyalkylmethacrylate), poly(saccharide), poly(a-hydroxy acid), poly(vinyl alcohol), polyphosphazene, polyoxazoline, poly(N-acryloylmorpholine), and combination of any of the foregoing." Upon information and belief, BAY 94 is comprised of a conjugate that is conjugated with PEG. Ex K at ¶ 69 (describing BAY 94 as comprising a conjugate that is "pegylated with a large 60 kDa PEG molecule"); Ex. N at 270 ("PEGylation is the covalent attachment of long-chained chemically activated polyethylene glycol (PEG) molecules to proteins.").

153. As a result of Bayer's wrongful acts, Plaintiffs will be substantially and irreparably harmed if Bayer is not enjoined from infringing the '831 patent. Plaintiffs have no adequate remedy at law.

154. As a result of Bayer's infringement, Plaintiffs will suffer damages and are entitled to recover from Bayer the damages in an amount to be determined through discovery and/or trial, but in an amount no less than a reasonable royalty.

155. As a result of Bayer's infringement, Plaintiffs are entitled to an award of attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs Baxalta Inc., Baxalta US, and Nektar pray for judgment against Defendant Bayer, and respectfully request the following relief:

1. A judgment that the '223 patent, the '421 patent, the '378 patent, the '536 patent, the '102 patent, the '259 patent, and/or the '831 patent have been infringed and will be infringed by Bayer;

2. A judgment for an injunction enjoining Bayer, and its officers, agents, servants, and employees, and those persons acting in active concert or participation with all or any of them from manufacturing, using, offering to sell, or selling BAY 94 within the United States, or importing BAY 94 into the United States, prior to the expiration of the '223 patent, the '421 patent, the '378 patent, the '536 patent, the '102 patent, the '259 patent, and/or the '831 patent pursuant to 35 U.S.C. § 283;

3. To the extent that Defendant has or will commercially manufacture, use, offer to sell, sell, or import BAY 94 into the United States prior to the expiration of the '223 patent, the '421 patent, the '378 patent, the '536 patent, the '102 patent, the '259 patent, and/or the '831 patent, including any extensions, a judgment pursuant to 35 U.S.C. § 284 awarding Plaintiffs monetary relief together with interest, costs, expenses and disbursements.

4. An award of all other damages as are appropriate under 35 U.S.C. § 284;

5. A judgment that this is an exceptional case and that Plaintiffs be awarded their attorneys' fees incurred in this action pursuant to 35 U.S.C. § 285;

6. Costs and expenses in this action; and

7. Such other and further relief as the Court deems just and appropriate.

DEMAND FOR JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs demand a trial by jury on all claims and issues so triable.

/s/ Kelly E. Farnan
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