IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BAYER HEALTHCARE LLC, Plaintiff, v. BAXALTA INCORPORATED, BAXALTA US INC., and NEKTAR THERAPEUTICS, Defendants.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT

Plaintiff Bayer HealthCare LLC ("Bayer"), by and through its undersigned attorneys, hereby commences this action for patent infringement against Defendants Baxalta Incorporated ("Baxalta Inc."), Baxalta US Inc. ("Baxalta US"), and Nektar Therapeutics ("Nektar") (collectively, "Defendants") and alleges as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*

THE PARTIES

2. Plaintiff Bayer is a corporation organized under the laws of the State of Delaware, having its principal place of business at 100 Bayer Boulevard, Whippany, New Jersey, 07981.

3. Defendant Baxalta Inc. is a corporation organized under the laws of the State of Delaware, having its principal place of business at 1200 Lakeside Drive, Bannockburn, Illinois, 60015.

4. Defendant Baxalta US is a corporation organized under the laws of the State of Delaware, having its principal place of business at 1 Baxter Way, Westlake Village, California, 91362.

5. Defendants Baxalta Inc. and Baxalta US were incorporated in the State of Delaware prior to their separation, by way of a spin-off, from Baxter International Inc. ("Baxter").

6. Upon information and belief, Defendant Baxalta US is a wholly-owned subsidiary of its parent company Defendant Baxalta Inc.

7. Upon information and belief, Defendant Baxalta US acts at the direction, control, and for the direct benefit of Defendant Baxalta Inc. and is controlled and/or dominated by Baxalta Inc.

8. Defendant Nektar is a corporation organized under the laws of the State of Delaware, having its principal place of business at 455 Mission Bay Boulevard South, San Francisco, California, 94158.

JURISDICTION AND VENUE

9. This is an action arising under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, and over which this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

10. This Court has general jurisdiction over Baxalta Inc., Baxalta US, and Nektar because each is a Delaware corporation.

11. This Court has personal jurisdiction over Baxalta Inc., Baxalta US, and Nektar because they have committed acts of direct and indirect patent infringement in this forum by the distribution and sale of infringing products without authority from Bayer, a Delaware

corporation. In addition, Nektar has availed itself of the rights, benefits, and privileges of this Court by consenting to jurisdiction in this Judicial District in prior litigation. *See, e.g., Green Cross Corp. v. Nektar Therapeutics*, 1:09-cv-00160-RGA.

12. Venue is proper in this Judicial District under 28 U.S.C. §§ 1391(b) and (c) and 1400(b).

FACTS

13. Plaintiff Bayer is a global life science company whose lineage traces back over 150 years. Bayer focuses on the research and development of innovative drug treatments in numerous therapeutic areas, including hematology.

14. Bayer's innovative research and development in the hematology field has focused on the treatment of Hemophilia A, a genetic blood coagulation disorder that affects approximately 400 newborn babies each year in the United States and over 400,000 people worldwide. Patients suffering from Hemophilia A are afflicted with a deficiency of the functional human Factor VIII protein, which is critical for proper blood coagulation and the control of bleeding. These 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 patients can suffer severe and even fatal bleeding episodes.

15. Treatment for Hemophilia A patients includes prophylactic administration of Factor VIII, as well as intravenous injections in response to a bleeding episode. However, in humans, Factor VIII has a relatively short half-life of approximately 11 hours. Because of this short half-life, patients who are required to receive prophylactic intravenous Factor VIII must be injected as frequently as three times or more per week.

16. Bayer is a leader in the research and development efforts related to understanding the role of Factor VIII and treatments for Hemophilia A. Bayer has developed and markets several Factor VIII replacement therapies in the United States. Kogenate®, Kogenate® FS, and Kovaltry® are all Antihemophilic Factor VIII products produced by Bayer using recombinant DNA technology. Kogenate® was one of the first recombinant Factor VIII products approved for use in the United States by the U.S. Food and Drug Administration ("FDA") in 1993. Kogenate® FS, an improved Kogenate® product formulation, was approved by the FDA in 2000. Kovaltry®, which provides for less frequent prophylactic dosing in certain patients, was approved by the FDA in March 2016.

17. Bayer has continued to devote substantial research and development resources into improving Hemophilia A treatments, including by the use of pegylation technology. Pegylation is a method by which chains of polyethylene glycol polymers ("PEGs") are attached, or conjugated, to active biologic or chemical entities in the hope that certain unique properties will be imparted to a therapeutic product. Bayer has discovered, *inter alia*, that site-directed pegylation can extend the half-life of Factor VIII by slowing the body's clearance of the Factor VIII protein, thus reducing the frequency of injections required to control bleeding in Hemophilia A patients.

THE PATENT IN SUIT AND ITS FAMILY

18. United States Patent No. 9,364,520 ("the '520 patent"), entitled "Factor VIII Conjugates" was duly and legally issued by the United States Patent and Trademark Office ("USPTO") on June 14, 2016. The claims of the '520 patent are directed to, *inter alia*, full-length Factor VIII that is pegylated at its B-domain site, and compositions thereof. Bayer is the

assignee and owner of the '520 patent. A true and correct copy of the '520 patent is attached hereto as Exhibit A.

19. The '520 patent issued from United States Patent Application No. 12/540,703 ("the '520 application"), which was filed with the USPTO on August 13, 2009 and published on April 1, 2010. The '520 application is a continuation of U.S. Application No. 11/273,896 ("the '520 parent application"), which was filed November 14, 2005 and published on June 1, 2006. The '520 parent application shares the same specification as the '520 patent and claims priority to U.S. Provisional Application No. 60/627,277 ("the Bayer provisional application"), which was filed on November 12, 2004.

20. The '520 application was reviewed by the United States Patent Trial and Appeal Board ("the Board"). In the course of reviewing this application, the Board considered a patent cited by the Examiner as prior art and assigned on its face to Defendant Nektar that is directed to "random pegylation," i.e., pegylation that is not directed to the B-domain of Factor VIII. The Board's decision in favor of Bayer led to the issuance of the '520 patent over the Nektar patent. A true and correct copy of the Board's decision is attached as Exhibit B.

21. Bayer has also filed patent applications that are related to the '520 patent at the European Patent Office, including a counterpart to the '520 patent. These European applications share the same specification disclosures as the '520 patent and claim priority to the Bayer provisional application.

ADYNOVATE® – THE INFRINGING PRODUCT

22. Upon information and belief, a Nektar-related entity was a party to a September 26, 2005 Exclusive Research, Development, License and Manufacturing and Supply Agreement with Baxter-related entities to develop and sell pegylated protein candidates for

treatment of Hemophilia. In December 2007, that agreement was amended, such that the Nektar-related entity granted the Baxter-related entities an exclusive license to Nektar's pegylation technology.

23. Upon information and belief, Baxter later spun-off Baxalta Inc. and Baxalta US as separate corporate entities.

24. Upon information and belief, pursuant to the September 26, 2005 agreement, Nektar worked with Baxter, Baxalta US, and/or Baxalta Inc. to develop, manufacture, and/or market an extended half-life recombinant Factor VIII treatment for Hemophilia A based on the Advate® (Antihemophilic Factor (Recombinant)) Factor VIII product. Advate® was approved by the FDA on July 25, 2003, and is indicated for the prevention and control of bleeding episodes in patients with Hemophilia A. Upon information and belief, Nektar applied pegylation technology to the Advate® product, which led to the development of Adynovate®, which during product development was referred to as "BAX 855."

25. Baxalta US currently owns Biologics License Application ("BLA") No. 125566 for Adynovate® (Antihemophilic Factor (Recombinant), PEGylated), which was approved by the FDA on November 13, 2015. A true and correct copy of Baxalta Inc.'s press release announcing FDA approval of Adynovate® is attached as Exhibit C. Adynovate® is indicated for on-demand treatment and control of bleeding episodes, and for routine prophylaxis to reduce the frequency of bleeding episodes in adults and adolescents aged 12 years and older with Hemophilia A. According to the Adynovate® website, Adynovate® "is the first and only treatment with an extended circulating half-life built on Advate®" and offers a "simple, twice-weekly dosing schedule." A true and correct copy of the Adynovate® website, available at http://www.adynovate.com/, is attached as Exhibit D.

26. Upon information and belief, each of Baxalta Inc. and Baxalta US makes, uses, offers to sell, sells and/or imports pegylated Factor VIII conjugates, including Adynovate®, pursuant to its exclusive license agreement with Nektar. Upon information and belief, Nektar has supplied and will continue to supply PEGs and pegylation technology exclusively to Baxalta US and/or Baxalta Inc. as part of Defendants' collaboration to develop, make, use, offer for sale, sell, and/or import Adynovate®.

27. Adynovate® is manufactured at least at Baxalta US's facility located at 1700 Rancho Conejo Blvd, Thousand Oaks, California, 91320.

28. Baxalta Inc. and/or Baxalta US currently market Adynovate® throughout the United States, including in the State of Delaware.

29. One or more claims of the '520 patent cover Adynovate®.

THE BAYER/NEKTAR HISTORY

30. Bayer and Nektar entered into a "Research Agreement" ("the Agreement") on December 11, 2003. Under the Agreement, at Bayer's direction, Nektar agreed to attempt to pegylate Bayer's recombinant human Factor VIII proteins (both full length and B-domain deleted ("BDD") variants) using random pegylation.

31. The term of the Agreement ran for one year from the December 11, 2003 effective date.

32. In 2004, pursuant to the Agreement, 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.

33. The report included pegylation yield and degree of pegylation. The report did not include any information regarding Nektar's pegylation techniques.

34. Based on Nektar's report, Bayer determined that the samples were not commercially viable treatment options warranting further development with Nektar. The report indicated that Nektar's pegylation technology and the resulting samples suffered from, *inter alia*, deficient purification, unsatisfactory characterization of the degree of pegylation, and low pegylation yield. Because of these deficiencies, Bayer elected to not renew the Agreement and instead discontinued the relationship with Nektar upon conclusion of Nektar's work contemplated under the Agreement.

35. 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.

DEFENDANTS' AWARENESS OF BAYER'S PATENTS

36. In 2013, Bayer filed an action in civil court in Munich, Germany, seeking co-ownership rights in certain of Nektar's pending European patent filings concerning pegylated recombinant Factor VIII compounds and related patents that reflect information Nektar obtained through communications from Bayer.

37. After Bayer filed its action in Germany, 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. These applications are from the same family and share the same specification as the '520 patent. Nektar relies, in part, on the Agreement in claiming that it is entitled to rights in these applications, an allegation Bayer disputes for the reasons set forth in paragraphs 30-35, among others.

38. In addition, Nektar is listed as the assignee on two issued U.S. Patents and four U.S. Patent Applications that cite the '520 parent application. The '520 parent application was

cited by Nektar and/or the Patent Examiner during prosecution of Nektar's U.S. Patent Nos. 8,586,711 and 9,347,054 and U.S. Patent Application Nos. 12/795,461; 12/638,874; 12/638,744; and 12/638,904. Nektar also had specific knowledge of the '520 parent application because the claims in one of Nektar's patent applications were rejected as being unpatentable over the '520 parent application.

39. Upon information and belief, and prior to the filing of this Complaint, Nektar has been familiar with and knew of Bayer's patent portfolio related to the '520 patent and its disclosures therein, including the '520 parent application and the Bayer provisional application.

40. Upon information and belief, and at least since the date of the filing of this Complaint, Nektar knew or should have known that its conduct related to the Adynovate® product pursuant to its exclusive partnership with Baxalta US and Baxalta Inc. would induce and contribute to Baxalta US and Baxalta Inc.'s infringement of Bayer's patents related to Factor VIII conjugates, including the '520 patent.

COUNT 1 – INFRINGEMENT OF THE '520 PATENT

41. Bayer repeats and realleges each of the foregoing paragraphs as if fully set forth herein.

42. Baxalta US and Baxalta Inc. have directly infringed and continue to directly infringe one or more claims of the '520 patent, either literally or under the doctrine of equivalents, by making, using, offering for sale, selling and/or importing Adynovate® in the United States and in this Judicial District without authority, in violation of 35 U.S.C. § 271.

43. Adynovate® satisfies each and every element of one or more claims of the '520 patent, for example, and without limitation, claims 1 and 9.

44. Claim 1 of the '520 patent recites:

> An isolated polypeptide conjugate comprising
> a functional factor VIII polypeptide and one or more
> biocompatible polymers,
> wherein the functional factor VIII polypeptide comprises the
> amino acid sequence of SEQ ID NO: 4 or an allelic variant
> thereof and has a B-domain, and further
> wherein the biocompatible polymer comprises polyalkylene oxide
> and is covalently attached to the functional factor VIII
> polypeptide at the B-domain.

45. Adynovate® satisfies the following limitations of claim 1 of the '520 patent:

A. "[A] functional factor VIII polypeptide and one or more biocompatible polymers." According to its package insert, Adynovate® "increases plasma levels of factor VIII and can temporarily correct the coagulation defect in hemophilia A patients." (Ex. E at sec. 12.2; *see also id.* at 1 (Adynovate® is indicated for "[o]n-demand treatment and control of bleeding episodes" and "[r]outine prophylaxis to reduce the frequency of bleeding episodes.").) Additionally, an article coauthored by Baxter and Nektar researchers concludes that "[t]he functional properties of BAX 855 are fully retained . . . Functionality and improvement of pharmacodynamic and pharmacokinetic properties was demonstrated in relevant animal models for human haemophilia A." (Ex. F at S37.) Adynovate® also contains one or more PEGs, which are biocompatible polymers. (Ex. E at sec. 11; Ex. A at col.8 ll.41-43.);

B. "[W]herein the functional factor VIII polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or an allelic variant thereof and has a B-domain." The amino acid sequence of Adynovate® is identical to SEQ ID NO: 4. (Ex. G at 50-51; Ex. H at 1-2.) In addition, Adynovate® contains a B-domain. (Ex.

I at 124 ("Rurioctocog alfa pegol (BAX 855, Adynovate®; Baxalta, Bannockburn, IL, USA) is a full-length recombinant FVIII with a 20 kDa branched PEG covalently bound to the B-domain region and has recently been approved for use in the US."); *see also* Ex. G at 50-51 (showing amino acid sequence of Adynovate® that includes the B-domain region); Ex. H at 1-2.); and

C. "[W]herein the biocompatible polymer comprises polyalkylene oxide and is covalently attached to the functional factor VIII at the B-domain." Adynovate® contains the biocompatible polymer PEG, which is a polyalkylene oxide. (Ex. E at sec. 11; Ex. A at col.8 ll.41-43.) Adynovate® also contains PEG covalently attached to the B-domain of the functional Factor VIII. (Ex. F at S29; Ex. I at 124 (Adynovate® contains "a 20 kDa branched PEG covalently bound to the B-domain region").)

46. Claim 9 of the '520 patent recites:

> A pharmaceutical composition comprising
> (1) a therapeutically effective amount of a monopegylated polypeptide conjugate,
> wherein the monopegylated polypeptide conjugate comprises a functional factor VIII polypeptide and one polyethylene glycol polymer,
> the functional factor VIII polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or an allelic variant thereof and has a B-domain, and
> the polyethylene glycol is covalently attached to the functional factor VIII at the B-domain; and
> (2) a pharmaceutically acceptable adjuvant.

47. Adynovate® satisfies the following limitations of claim 9 of the '520 patent:

A. "[A] therapeutically effective amount of a monopegylated polypeptide conjugate." According to its package insert, Adynovate® "is a recombinant full-length human coagulation factor VIII (2,332 amino acids with a molecular weight (MW) of 280 kDa) covalently conjugated with one or more molecules of polyethylene glycol (MW 20 kDa)." (Ex. E at sec. 11.) Thus, upon information and belief, Adynovate® is a mixture of recombinant full-length human coagulation Factor VIII modified with varying degrees of a branched PEG, one of which is monopegylated Factor VIII having therapeutic activity;

B. "[W]herein the monopegylated polypeptide conjugate comprises a functional factor VIII polypeptide and one polyethylene glycol polymer." Adynovate® contains a functional Factor VIII polypeptide conjugated with one PEG. (Ex. E at sec. 12.2; *id.* at 1; *id.* at sec. 11; Ex. F at S37; Ex. I at 124.);

C. "[T]he functional factor VIII polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or an allelic variant thereof and has a B-domain." Adynovate® has an amino acid sequence identical to SEQ ID NO: 4. (Ex. G at 50-51; Ex. H at 1-2.) Adynovate®'s amino acid sequence includes the B-domain. (Ex. I at 124; *see also* Ex. G at 50-51; Ex. H at 1-2.);

D. "[T]he polyethylene glycol is covalently attached to the functional factor VIII at the B-domain." Adynovate® contains PEG covalently attached to the B-domain of the functional Factor VIII. (Ex. F at S29; Ex. I at 124.); and

E. "[A] pharmaceutically acceptable adjuvant." Adynovate®'s package insert states that the finished product contains pharmaceutically acceptable adjuvants such as "excipients and stabilizers." (Ex. E at sec. 11.) These adjuvants include, *inter alia*, sterilized water, sugar (mannitol), and salt (sodium chloride). (*Id.*)

COUNT 2 – INDUCED INFRINGEMENT OF THE '520 PATENT UNDER 35 U.S.C. § 271(b)

48. Bayer repeats and realleges each of the foregoing paragraphs as if fully set forth herein.

49. Upon information and belief, Nektar has induced and will continue to induce Baxalta US and Baxalta Inc.'s direct infringement of the '520 patent as set forth under Count 1 above.

50. Upon information and belief, Nektar knew or should have known of the '520 patent and intended that Baxalta US and Baxalta Inc. infringe the '520 patent.

51. Upon information and belief, Nektar knew or should have known of the existence of the '520 patent because Nektar was monitoring the '520 patent family, *inter alia*, by virtue of its 2015 patent action in the courts of Munich, Germany.

52. Upon information and belief, Nektar knew or should have known about the existence of Bayer's '520 patent because Nektar prosecuted patents and applications in which the '520 parent application was cited, as set forth in paragraphs 38 and 39 above.

53. Upon information and belief, Nektar knew or should have known that its actions with Baxalta US and Baxalta Inc., related to pegylation of Factor VIII, would lead to Baxalta US and Baxalta Inc.'s infringement of the '520 patent. For instance, Nektar co-authored an article

with Baxter concerning their joint development of BAX 855, reporting that BAX 855 is a full-length Factor VIII molecule pegylated at the B-domain that exhibits a prolonged half-life.

COUNT 3 – CONTRIBUTORY INFRINGEMENT OF THE '520 PATENT UNDER 35 U.S.C. § 271(c)

54. Bayer repeats and realleges each of the foregoing paragraphs as if fully set forth herein.

55. Upon information and belief, Nektar has contributed and will contribute to Baxalta US and Baxalta Inc.'s direct infringement of the '520 patent as set forth under Count 1 above.

56. Nektar knew or should have known about the existence of Bayer's '520 patent as set forth under Count 2 above.

57. The PEGs and pegylation technology provided by Nektar to Baxalta US and Baxalta Inc. for the manufacture, use, offer for sale, sale, and/or importation of Adynovate® are a material part of the Adynovate® product because pegylation of Advate® on behalf of Baxalta US and Baxalta Inc. results in the increased half-life of Adynovate®.

58. There are no other substantial noninfringing uses for the PEGs and pegylation technology provided by Nektar to Baxalta US and Baxalta Inc. for the manufacture, use, offer for sale, sale, and/or importation of Adynovate®, and the PEGs and pegylation technology are not staple articles or commodities of commerce. Upon information and belief, Nektar's exclusive license providing PEGs and pegylation technology to Baxalta US and Baxalta Inc. limits their use to Adynovate® only.

COUNT 4 – WILLFUL INFRINGEMENT OF THE '520 PATENT UNDER 35 U.S.C. § 284

59. Upon information and belief, Defendants' infringement of the '520 patent is willful and intentional under 35 U.S.C. § 284, rendering this case exceptional under 35 U.S.C. § 285, and entitling Bayer to enhanced damages and attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

60. Upon information and belief, Baxalta US and Baxalta Inc. knew or should have known that their conduct related to the development, manufacture, use, offer for sale, sale, and/or importation of the Adynovate® product constituted an unreasonable risk of infringement of at least one valid and enforceable claim of the '520 patent.

61. Baxalta US and Baxalta Inc.'s infringement continues to be willful, entitling Bayer to enhanced damages and attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

62. Upon information and belief, Nektar knew or should have known that its actions inducing and contributing to Baxalta US and Baxalta Inc.'s development, manufacture, use, offer for sale, sale, and/or importation of the Adynovate® product constituted an unreasonable risk of infringing at least one valid and enforceable claim of the '520 patent.

63. Nektar's infringement continues to be willful, entitling Bayer to enhanced damages and attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Bayer requests that the Court enter judgment in its favor and against Defendants Baxalta US, Baxalta Inc., and Nektar as follows:

A. A judgment that Defendants have infringed at least one claim of the '520 patent;

B. A judgment that the '520 patent is valid and enforceable;

C. An award to Bayer of damages adequate to compensate it for Defendants' past infringement and any continuing or future infringement, including at minimum reasonable royalties, together with interest, costs, expenses, and disbursements as justified under 35 U.S.C. § 284;

D. An award to Bayer of all other damages permitted by 35 U.S.C. § 284, including enhanced damages up to three times the amount of compensatory damages found;

E. Permanently enjoining Defendants, their officers, agents, servants, employees, attorneys, all parent and subsidiary corporations and affiliates, their assigns and successors in interest, and those persons in active concert or participation or privity with Defendants who receive notice of the injunction, from continuing acts of infringement of the '520 patent;

F. Finding that this is an exceptional case and awarding to Bayer its reasonable attorneys fees and costs pursuant to 35 U.S.C. § 285; and

G. Such other and further relief in law or equity as the Court deems just and appropriate.

DEMAND FOR JURY TRIAL

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

Dated: December 5, 2016

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