Bradford. J. Badke (*pro hac vice forthcoming*)
Sona De (SBN# 193896)
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
jbadke@sidley.com
sde@sidley.com
Telephone: (212) 839-5300
Facsimile: (212) 839-5599

Sue Wang (SBN# 286247)
SIDLEY AUSTIN LLP
555 California Street, Suite 2000
San Francisco, CA 94104
sue.wang@sidley.com
Telephone: (415) 772-1200
Facsimile: (415) 772-7400

Attorneys for Plaintiff Bayer HealthCare LLC

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

_____ DIVISION

BAYER HEALTHCARE LLC Plaintiff, vs. NEKTAR THERAPEUTICS, BAXALTA INCORPORATED, and BAXALTA US INC., Defendants.	Case No. _____ **COMPLAINT FOR DECLARATORY JUDGMENT OF PATENT NON-INFRINGEMENT AND INVALIDITY** DEMAND FOR JURY TRIAL

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

NATURE OF ACTION

1. This is an action arising under the Declaratory Judgment Act, 28 U.S.C. § 2201, *et seq*., and the United States Patent Act, 35 U.S.C. § 1, *et seq*. Bayer seeks a declaratory judgment that U.S. Patent No. 7,858,749 (Ex. 1, "the '749 patent") is invalid and not infringed by Bayer's Factor VIII replacement product BAY 94-9027 ("BAY 94").

THE PARTIES

2. Plaintiff Bayer is organized under the laws of the State of Delaware, having its principal place of business at 100 Bayer Boulevard, Whippany, New Jersey, 07981, and substantial facilities in this District at 800 Dwight Way, Berkeley, California, 94710.

3. 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.

4. 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.

5. 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.

6. 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").

7. Defendant Baxalta US is a wholly owned subsidiary of its parent company Defendant Baxalta Inc.

8. Upon information and belief, Baxalta Inc. is a wholly owned, indirect subsidiary of Shire plc.

9. 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.

JURISDICTION

10. This is an action arising under the Declaratory Judgment Act, 28 U.S.C. § 2201, *et seq*., and the United States Patent Act, 35 U.S.C. § 1, *et seq*.

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

12. This Court has personal jurisdiction over Nektar because it is domiciled in this District, has numerous, continuous, and systematic contacts with this District, and therefore has purposefully availed itself of the privilege of conducting activities within this District. Nektar houses its corporate offices and research and development laboratories in this District, and the '749 patent states on its face that it is situated by assignment to Nektar at its headquarters in this District in San Francisco, California. In addition, Nektar has submitted to the jurisdiction of this Court on at least one occasion: *In re Application of Bayer Healthcare, LLC*, No. 3:14-mc-80138 (N.D. Cal. May 14, 2014).

13. This Court has personal jurisdiction over Baxalta Inc. and Baxalta US because they purposefully direct their activities to residents of this District, have numerous, continuous, and systematic contacts with this District, and therefore, have purposefully availed themselves of the privilege of conducting activities within this District. Upon information and belief, Baxalta Inc. and Baxalta US employ individuals and have multiple manufacturing facilities in California, including in this District at 1978 West Winton Avenue, Hayward, California, 94545.

14. Upon information and belief, Baxalta Inc. and Baxalta US are parties to an exclusive license agreement with Nektar, pursuant to which Nektar granted Baxalta Inc. and Baxalta US exclusive rights to the family of patents and applications that includes the '749 patent ("the '749 patent family"). Upon information and belief, under the terms of the exclusive license agreement, Nektar expressly or impliedly transferred its rights in the '749 patent family to Baxalta Inc. and Baxalta US in at least the field of treatment of hemophilia A or pegylated Factor VIII.

15. Upon information and belief, pursuant to the exclusive agreement, Baxalta Inc. and Baxalta US purchase materials (e.g., polyethylene glycol polymers ("PEG")) from Nektar

that are manufactured in this District for a portion of the product supply chain for Adynovate®, Baxalta Inc. and Baxalta US's pegylated Factor VIII replacement product. In exchange, Baxalta Inc. and Baxalta US are responsible for development and commercialization of Adynovate® and remit substantial royalty payments to Nektar in this District in the form of: escalating royalties between 4-6 percent on global net revenue of Adynovate® up to $1.2 billion in revenue, 13% royalty for revenue above $1.2 billion, and additional tiered revenue milestone payments based upon global net revenue of Adynovate®.

16. Baxalta Inc. and Baxalta US have also purposefully directed their activities at consumer-residents of this forum in a systematic and continuous manner. Upon information and belief, Baxalta Inc. and/or Baxalta US sell and market their products, including Adynovate®, throughout this District and the State of California.

17. Baxalta US has appointed a registered agent in this state to accept service of process on its behalf and is therefore subject to service in California.

VENUE

18. Venue is proper in this District under 28 U.S.C. §§ 1391(a), (b), (c), and (d) because Nektar, Baxalta Inc., and Baxalta US are subject to this Court's personal jurisdiction by virtue of their continuous and systematic contacts with this District. In addition, the '749 patent states on its face that it is situated by assignment to Nektar at its headquarters in this District in San Francisco, California.

19. Venue is also proper in this District because Bayer maintains a substantial site for research, development, and manufacture of biological products in Berkeley, California.

INTRADISTRICT ASSIGNMENT

20. For purposes of intradistrict assignment under Civil Local Rules 3-2(c) and 3-5(b), this Intellectual Property Action will be assigned on a district-wide basis.

FACTUAL BACKGROUND

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

22. Bayer has focused its innovative research and development in the hematology field 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, a complex protein that is critical for proper blood coagulation and 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 treatment includes both prophylactic administration of Factor VIII replacement products as well as intravenous injections in response to a bleeding episode.

23. 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 several Factor VIII replacement therapies in the United States, including its recombinant antihemophilic Factor VIII products Kogenate®, Kogenate® FS, and Kovaltry®. Kogenate® was one of the first recombinant Factor VIII products approved 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.

24. In humans, Factor VIII has a relatively short half-life of approximately 11 hours. Because of this short half-life, patients who require prophylactic Factor VIII replacement therapy are required to receive Factor VIII infusions up to three times per week, and sometimes as often as every day. Such frequent dosing limits the ability of hemophilia A patients to lead dynamic, active lifestyles, especially for adolescents and young adults. The demanding nature of prophylactic Factor VIII treatment may also contribute to patient noncompliance, which can lead to serious adverse consequences, including fatal bleeding episodes. Therefore, increasing the half-life of Factor VIII treatments to reduce the frequency of infusions is of utmost importance to hemophilia A patients, their treating physicians, and researchers.

25. Since introducing Kogenate® in 1993, Bayer has continued to devote substantial research and development resources to improving hemophilia A treatments, including by implementing pegylation technology to increase the half-life of Factor VIII replacement products in order to reduce the frequency of infusions and reduce immunogenicity. Pegylation is a method by which PEG molecules are attached to active biologic or chemical entities in an effort to impart certain unique properties, such as potentially preventing degradation of the therapeutic product to extend its half-life.

26. Factor VIII, however, is a very large and complex protein that is unique in structure and function. As a result, it has presented challenging issues related to extending its half-life through pegylation. Factor VIII interacts with a host of additional enzymes and proteins in a particular sequence of biochemical events that leads to blood coagulation. To begin this cascade of reactions, thrombin, a plasma enzyme, must first activate Factor VIII; thereafter, the activated Factor VIII interacts sequentially with a number of additional enzymes leading eventually to the generation of fibrin, which forms the lattice responsible for blood clotting. Therefore, if a PEG molecule is attached to Factor VIII at a location that must interact with any of the other chemicals involved in the clotting cascade, the pegylated Factor VIII may lose a significant amount of coagulation activity.

27. In the 1990s, small PEG molecules (e.g., ≤ 5 kDa) were known to extend the half-life of therapeutic candidates that were less complex and much smaller than Factor VIII. At that time it was generally believed that Factor VIII, due to its complexity and large size, would require many small (e.g., ≤ 5 kDa) PEG molecules to shield it from degradation in order to extend its half-life. However, this approach resulted in a loss of Factor VIII's coagulation activity and did not extend the active Factor VIII's half-life by a satisfactory amount of time.

BAYER'S CONFIDENTIAL FACTOR VIII PEGYLATION RESEARCH AND DISCLOSURE TO NEKTAR

28. Despite the failure of others to achieve success with pegylated Factor VIII, Bayer in the early 1990s began its own program to develop a pegylated Factor VIII replacement product with the goal of improving half-life and reducing immunogenicity while retaining

coagulation activity. This work occurred at Bayer's biologics research center in Berkeley, California.

29. By 1993, Bayer became the first to discover and make a pegylated Factor VIII using only one large PEG (e.g., ≥ 20 kDa) that provided an extended half-life while retaining coagulation activity, an unexpected result that ran contrary to conventional wisdom.

30. For this work, Bayer sought out PEG suppliers who could provide large PEGs because such large PEG molecules were not readily available. One such supplier of PEGs was Nektar's predecessor in interest, Shearwater Corporation ("Shearwater"), located in Huntsville, Alabama. Shearwater manufactured and sold small PEG molecules as catalog items, but was capable of providing by custom order the large PEG molecules that Bayer needed.

31. Upon information and belief, Bayer (at this time known as Miles Laboratories in the United States) and Shearwater entered into a confidentiality agreement in 1993, and Shearwater began providing Bayer with custom-made larger PEG molecules in consultation with Shearwater's founder, Dr. J. Milton Harris, who was a scientist knowledgeable about pegylation chemistry.

32. The same year, Bayer and Dr. Harris entered into a consulting agreement so that Bayer could disclose its confidential research on Factor VIII to Dr. Harris. The term of the consulting agreement between Bayer and Dr. Harris continued through at least 1995.

33. Over the course of the consultancy, Dr. Harris and Bayer scientists regularly spoke by phone and in person. During these discussions, Bayer disclosed to Dr. Harris the details of its pegylated Factor VIII research and discoveries. As a result, Dr. Harris learned, for example, of Bayer's discovery that attaching large PEG molecules (e.g., ≥ 20 kDa) at fewer binding sites (e.g., one) increases Factor VIII's half-life while coagulation activity is retained.

34. Upon information and belief, Dr. Michael Bentley joined Shearwater in 1997 as the head of its research and drug development program while Dr. Harris was still serving as president of the company.

35. Upon information and belief, Dr. Bentley became aware of certain details of Bayer's Factor VIII pegylation research and development while employed at Shearwater with Dr. Harris.

36. In its ongoing effort to perfect its Factor VIII pegylation technology, on June 17, 1998, Bayer entered into a second Mutual Non-Disclosure Agreement with Shearwater, which Dr. Harris signed on behalf of Shearwater. Upon information and belief, Dr. Bentley remained employed by Shearwater at this time.

37. Around the same time, Bayer began consulting with another supplier of PEGs, PolyMASC Pharmaceuticals PLC ("PolyMASC"). Bayer met and corresponded with PolyMASC concerning Bayer's pegylation work on Factor VIII and entered into a Research Agreement with PolyMASC in 1999 in furtherance thereof. The PolyMASC Research Agreement confidentiality provisions limited the use of all information and materials provided by Bayer to uses solely contemplated under the Agreement. Over the course of this business relationship, Bayer shared with PolyMASC its confidential information and discoveries concerning Bayer's long-standing research and discoveries concerning pegylated Factor VIII.

38. Upon information and belief, Bayer's confidential information concerning its pegylated Factor VIII research and discoveries was disclosed to the PolyMASC Director of Commercial Development, Dr. Stephen Charles, a scientist and inventor on several pegylation patents.

39. Upon information and belief, after learning the details of Bayer's pegylation work on Factor VIII, Dr. Charles left PolyMASC to join Drs. Harris and Bentley at Shearwater as Vice President of Corporate Development.

40. Upon information and belief, Drs. Harris, Bentley, and Charles all had scientific knowledge of pegylation technology and would have had a keen interest in understanding and making use of the confidential Bayer discoveries concerning extending the half-life of Factor VIII through pegylation.

41. In 2001, Inhale Therapeutics Systems, Inc. ("Inhale") acquired Shearwater.

42. Upon information and belief, Dr. Mary Bossard joined Shearwater in early October of 2002.

43. Upon information and belief, Drs. Harris, Bentley, Charles, and Bossard worked together for Shearwater in Huntsville, Alabama, from 2002 to at least 2003.

44. Upon information and belief, Dr. Bossard had not worked with Factor VIII or on pegylating Factor VIII prior to joining Shearwater.

45. Upon information and belief, Dr. Bossard's early work with Shearwater (and eventually Nektar) involved traveling with business teams to sell Shearwater's catalog of small PEG molecules.

46. In 2003, Inhale changed its name to Nektar Therapeutics ("Nektar"), while Shearwater changed its name to Nektar Therapeutics AL Corporation and later merged into its parent corporation, Nektar.

47. Dr. Harris served as president and later as chief scientific officer of Nektar, and Dr. Bentley headed Nektar's research group and started its drug development program. Dr. Charles became vice president of business development & alliance management at Nektar. Dr. Bossard's title at Nektar was senior director of science and technology.

48. Upon information and belief, while Nektar was knowledgeable about pegylation generally, it had very limited, if any, expertise with pegylating Factor VIII prior to at least February 26, 2003, independent of the knowledge that Drs. Harris, Bentley, and Charles learned from Bayer.

49. As of 2003, Bayer continued working to refine its process to commercialize a long-acting pegylated Factor VIII replacement therapy. As a result, Bayer once again renewed its relationship with Shearwater (now known as Nektar) to build on Bayer's own extensive confidential research work on pegylating Factor VIII.

50. On February 12, 2003, Bayer's legal predecessor-in-interest, Bayer Corporation, signed a confidential disclosure agreement ("CDA") with Nektar to enable Bayer once again to share its proprietary research information with Nektar. Dr. Charles, who had been employed by

PolyMASC and then Shearwater with Drs. Harris, Bentley, and Bossard, signed the non-disclosure agreement on behalf of Nektar.

51. Upon information and belief, Nektar, like its predecessor Shearwater since 1993, was primarily a catalog business that provided PEG reagents to pharmaceutical companies for conjugation work but did not carry out de novo drug discovery.

NEKTAR'S MISAPPROPRIATION OF BAYER'S CONFIDENTIAL INFORMATION FOR PATENT FILINGS

52. Within only a few months after Dr. Bossard joined Shearwater and only two weeks after signing the CDA with Bayer, on February 26, 2003, Nektar secretly filed Provisional Patent Application No. 60/450,578 (the "Provisional Application"), to which the '749 patent and '749 patent family claim priority. Drs. Bossard and Bentley are listed as the only inventors of the Provisional Application. Nektar did not inform Bayer of this secret filing.

53. Upon information and belief, this Provisional Application is based on information learned from Bayer by Drs. Harris, Charles, Bentley, and Bossard pursuant to Bayer's confidential collaborations with Shearwater, PolyMASC, and/or Nektar over a period of years, including Bayer's discovery of the efficacy of using fewer (e.g., one) large PEG molecules (e.g., $\geq$ 20 kDa) to pegylate Factor VIII.

54. Upon information and belief, Nektar did not have access to Factor VIII at the time it filed its Provisional Application.

55. Evidencing Nektar's lack of practical expertise with pegylating the complex Factor VIII protein, the Provisional Application does not contain any data for any of the examples disclosed therein, which are drafted in the present tense, as opposed to the past tense, demonstrating that the disclosed experiments had not been performed.

56. On December 11, 2003, Bayer entered into a Research Agreement (the "Agreement") with Nektar, which described the object of the parties' work as increasing the half-life of Factor VIII while at the same time preserving its activity levels. The Agreement contained provisions to protect Bayer's confidential information and limit the use and disclosure of any such confidential information to activities contemplated under the Agreement on a need-

to-know basis. Dr. Charles again signed this Agreement on behalf of Nektar. Nektar designated Dr. Bossard as its official correspondent for the project, such that all communications between Bayer and Nektar were to be with Dr. Bossard.

57. Despite having secretly filed the Provisional Application claiming the efficacy of pegylating Factor VIII with larger PEG molecules at fewer binding sites, Nektar sought to deceive Bayer by stating in the Plan of Research attached to the Agreement that more than one small PEG attached to "multiple subunits" on the complex Factor VIII protein may be required to meet Bayer's stated goals i.e., to extend half-life of Factor VIII while retaining its coagulation activity.

58. Notwithstanding Nektar's misrepresentations about the number and size of PEGs required to achieve Bayer's goals, Bayer instructed Nektar to pegylate Factor VIII according to Bayer's preferences as set forth in the Agreement and Plan of Research, including, *inter alia*, attachment of a large PEG (≥ 30 kDa) to Factor VIII, consistent with Bayer's earlier discoveries regarding the efficacy of mono-pegylated Factor VIII using a large PEG.

59. Pursuant to the Agreement, in early 2004, Bayer sent Nektar batches of recombinant Factor VIII, including B-domain deleted ("BDD") and full-length Factor VIII. Recombinant technology allows for production of proteins in large quantities using cells engineered to contain the gene encoding the protein of interest. BDD Factor VIII is a type of Factor VIII in which most or all of a segment of Factor VIII, known as the "B domain" has been removed, whereas full-length Factor VIII refers to a Factor VIII protein in which the B domain has been retained.

60. During this time, Bayer was in regular communication with Nektar about the agreed-upon work and testing through Nektar's designated correspondent, Dr. Bossard.

61. In February 2004, Nektar updated Bayer regarding its efforts to achieve Factor VIII pegylation using a large PEG molecule. On February 26, 2004, Nektar indicated that the PEGylation of Factor VIII was not very promising with regard to binding a large PEG molecule to the amino acid cysteine of Factor VIII. Notwithstanding this representation, on the same day,

unbeknownst to Bayer, Nektar secretly filed Patent Application No. 10/789,956 ("the '956 Application"), which is a continuation of the secret Provisional Application.

62. The '956 Application included new data and examples absent from the original Provisional Application and, upon information and belief, is based on the discoveries that Nektar learned from Bayer, e.g., the use of fewer (e.g., one) large PEG molecules (e.g., ≥ 20 kDa) to pegylate Factor VIII. Claim 1 of the '956 Application recited "[a] composition comprising a plurality of conjugates each conjugate having one to 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 greater than 5,000 Daltons to about 150,000 Daltons."

63. Subsequently, beginning in late-March through August 2004, Nektar provided to Bayer certain samples of recombinant human Factor VIII (full length and BDD) purportedly pegylated at cysteine and lysine amino acids, as well as a report corresponding to the work performed. The report included pegylation yield and degree of pegylation. The report did not include any information regarding Nektar's pegylation techniques.

64. 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 Nektar's inability to provide a reliable pegylation technique for Factor VIII and Bayer's own successful Factor VIII pegylation research carried out independently of Nektar, Bayer elected not to renew the Agreement and instead discontinued the relationship with Nektar upon conclusion of the work contemplated under the Agreement.

BAYER'S SUCCESSFUL DEVELOPMENT OF ITS LONG-ACTING, PEGYLATED FACTOR VIII

65. Bayer independently pursued its own Factor VIII pegylation research and development before, during, and after its multiple interactions with Shearwater and Nektar, dating back to the early 1990s when it began its Factor VIII pegylation research. Bayer filed its own patent applications in the United States and Europe based on its Factor VIII pegylation research and was granted, *inter alia*, U.S. Patent No. 9,364,520 in 2016.

66. Bayer's efforts culminated in the development of BAY 94, a pegylated recombinant human Factor VIII with extended half-life engineered to prolong duration of effect while preserving full coagulation activity. Bayer filed its Biologics License Application ("BLA") No. 125661 for BAY 94 with the FDA on August 30, 2017, seeking approval for the treatment of hemophilia A.

67. Bayer invented and developed BAY 94 in this District at its Berkeley, California research facility.

68. The sustained therapeutic effect of BAY 94 allows for less frequent dosing, thus reducing treatment burden and the potential to improve quality of life for hemophilia A patients. Early preclinical analysis of BAY 94 showed promising results, such as retained Factor VIII activity *in vitro* and improved half-life in animal models, which were later confirmed in clinical trials. Ex. 2 at 272-74 (referring to "K1804C," the BDD Factor VIII cysteine variant that is pegylated to make BAY 94); Ex. 3 at 490, 494. A recent clinical trial of BAY 94 demonstrated protection against bleeding with dosing intervals as infrequent as once per week, a marked improvement over currently available Factor VIII treatments in the U.S.

69. The active ingredient in BAY 94 is the recombinant BDD form of Factor VIII pegylated with a large 60 kDa PEG molecule, consistent with Bayer's discoveries in the 1990s. Ex. 2 at 271-272; Ex. 4 at 82 (entry for damoctocog alpha pegol, the nonproprietary name for BAY 94). The BAY 94 manufacturing process entails, *inter alia*, introduction of a cysteine and pegylation of a BDD Factor VIII protein with a 60 kDa PEG molecule attached via a thioether linkage to the introduced cysteine. Ex. 2 at 271; Ex. 4 at 82.

70. BAY 94 is to be administered intravenously and will be available as a lyophilized powder containing 250, 500, 1000, 2000, or 3000 International Units. 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.

71. After a quarter century of research, development, and testing requiring the expenditure of significant resources and commitments by Bayer, its groundbreaking Factor VIII

product, BAY 94, will offer a new treatment option for patients and potentially save lives worldwide.

NEKTAR, BAXALTA US, AND/OR BAXALTA INC. BENEFIT FROM THE MISAPPROPRIATION OF BAYER'S CONFIDENTIAL INFORMATION

72. Upon information and belief, while Bayer was paying Nektar to assist Bayer's efforts to perfect a commercially viable pegylated Factor VIII product, Nektar secretly sought out a partnership with Baxter, Baxalta Inc.'s corporate predecessor, to develop its own pegylated Factor VIII replacement therapy. At this time, Baxter and Bayer had competing Factor VIII replacement products.

73. Upon information and belief, Baxalta US Inc. and Baxalta Inc. are exclusive licensees of the '749 patent family by virtue of an Exclusive Research, Development, License and Manufacturing and Supply Agreement as amended and granted by Nektar to Baxter-related entities, originally executed on September 26, 2005, and transferred by assignment to Baxalta Inc. and/or Baxalta US on April 30, 2015.

74. Upon information and belief, Nektar worked with Baxalta Inc., Baxalta US, and/or Baxter to develop, manufacture, and/or market Adynovate®, an extended half-life recombinant Factor VIII (rFVIII) treatment for hemophilia A.

75. Upon information and belief, Nektar, its predecessors, and/or its employees improperly used and/or disclosed Bayer's confidential information to Baxalta Inc., Baxalta US, and/or Baxter to develop, commercialize, and/or manufacture Adynovate®.

76. Baxalta US currently owns BLA No. 125566 for Adynovate® (Antihemophilic Factor (Recombinant), PEGylated), which was approved by the FDA on November 13, 2015. Adynovate® is indicated in children and adults for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes.

77. Upon information and belief, Adynovate® is a full-length recombinant Factor VIII pegylated with a 20 kDa PEG, the same size PEG that Bayer disclosed to Dr. Harris in 1993.

78. Upon information and belief, Baxalta Inc. and/or Baxalta US are currently responsible for development and commercialization of Adynovate®, and Nektar supplies manufacturing materials for a portion of the supply chain to manufacture Adynovate®.

79. Upon information and belief, Baxalta Inc. and/or Baxalta US are recipients and beneficiaries of the confidential research work that Bayer performed beginning in the early 1990s through 2004 that was disclosed to Nektar, its predecessors, and/or its employees under confidentiality agreements that Nektar, its predecessors, and/or employees subsequently misrepresented as their own.

80. Upon information and belief, Nektar is a recipient and beneficiary of Bayer's confidential and proprietary research and discoveries that Bayer disclosed to Nektar, its predecessors, and/or its employees under confidentiality agreements that Nektar, its predecessors, and/or employees subsequently misrepresented as their own.

A DECLARATORY JUDGMENT IS WARRANTED BECAUSE THERE IS A SUBSTANTIAL CONTROVERSY OF SUFFICIENT IMMEDIACY AND REALITY

81. The totality of the circumstances demonstrate that there is a substantial controversy between Bayer and Defendants, whose legal interests are adverse to Bayer. The controversy is of sufficient immediacy and reality to warrant the issuance of a declaratory judgment that Bayer has not infringed and will not infringe any valid claim of the '749 patent and that the '749 patent is at least invalid. In addition, Bayer has made meaningful preparations to manufacture, use, offer to sell, and/or sell its BAY 94 product in the United States.

82. Bayer publicly described BAY 94 in 2010, including publication of Bayer's pegylation procedures and the results of various analyses of BAY 94. *See generally* Ex. 2.

83. Bayer and Nektar have litigated the rights to Factor VIII pegylation technology for many years. In 2013, Bayer filed an action in civil court in Munich, Germany, seeking ownership rights in certain of Nektar's pending European patent filings, which claim priority to the same Provisional Application from which the '749 patent derives. These European filings are based on Bayer's confidential Factor VIII research from the 1990s and 2000s that Nektar, its predecessors, and/or employees obtained through confidential communications with Bayer. In

connection with this German action, Bayer filed an *ex parte* Application for Discovery in Aid of Foreign Litigation Pursuant to 28 U.S.C. § 1782 in this Court, Docket No. 3:14-mc-80138, which was granted in May 2014.

84. 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 Bayer's Factor VIII pegylation research.

85. Bayer has actively researched and developed BAY 94, including through publicly known clinical trials. In 2010, Bayer announced its Phase 1 study to describe the pharmacokinetics of BAY 94. *See* Ex. 3. Based on the results of the Phase 1 study, Bayer designed and carried out an open-label, partially randomized Phase 2/3 trial, titled the "PROTECT VIII" trial, in 2012 to assess the effectiveness and safety of BAY 94 in previously treated patients at least 12 years of age with severe hemophilia A (ClinicalTrials.gov identifier: NCT01580293). The results of these studies were published and have been presented at numerous conferences. Upon information and belief, Baxalta Inc., Baxalta US, and Nektar are aware that Bayer has undertaken BAY 94 clinical trials to support its BLA submission.

86. Bayer contacted Nektar in an effort to come to an agreement that would avoid potential future litigation concerning BAY 94 and the '749 patent family, but Nektar refused. Upon information and belief, Baxalta Inc. and Baxalta US, as the exclusive licensees of this patent family, likewise refused to negotiate with Bayer.

87. In 2016, Bayer filed an action for patent infringement in the District of Delaware against Defendants, alleging that Adynovate® infringes Bayer's U.S. Patent No. 9,364,520.

88. In 2016, Bayer announced that it intended to file a BLA seeking regulatory approval of BAY 94 in mid-2017. Upon information and belief, Baxalta Inc., Baxalta US, and Nektar are aware of Bayer's plans to seek FDA approval of BAY 94 and that Bayer intended to do so before the end of 2017.

89. 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, Bayer has posted publicly available job postings for the

position of Director of Sales Hematology as recently as August 16, 2017. Bayer's sales force will begin actively marketing BAY 94 immediately upon receiving FDA approval.

90. It was announced publicly that Bayer submitted a BLA for BAY 94:

> Bayer AG today announced the submission of a Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA) for its long-acting site-specifically PEGylated recombinant human Factor VIII ([BAY 94]) for the treatment of Hemophilia A. The regulatory submission is essentially based on the results from the PROTECT VIII trial. In that trial, [BAY 94] showed protection from bleeds with dosing intervals when used prophylactically once every seven days, once every five days, and twice per week.
>
> "Since introducing Kogenate around 25 years ago, Bayer has been committed to continuously improving disease management for people living with Hemophilia A," said Dr. Joerg Moeller, member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Development. "The filing of [BAY 94] brings us one step closer to providing a therapeutic option with additional benefits for patients who decided to have a more active lifestyle."

News Release: Bayer Submits Biologics License Application in the U.S. for BAY94-9027 – a Long-Acting Factor VIII for the Treatment of Hemophilia A, Bayer AG Communications and Public Affairs (Berlin, Aug. 31, 2017) (available at http://press.bayer.com). Upon information and belief, Defendants know or will soon be aware of Bayer's submission of a BLA for BAY 94.

91. Bayer has a manufacturing facility in Berkeley, California, for the commercial manufacture of BAY 94 to accommodate the demand for BAY 94 following FDA approval. Upon information and belief, Defendants are aware of Bayer's manufacturing facility and capability to manufacture BAY 94 upon FDA approval.

92. According to standard industry practice, the FDA typically takes about one year to complete its review of a BLA. FDA approval of BAY 94 would permit Bayer to immediately offer to sell and sell the treatment within the United States, and Bayer expects to launch BAY 94 in the United States in the fourth quarter of 2018. Upon information and belief, Defendants are aware of the standard timeline for FDA approval and Bayer's intent to launch BAY 94 in the fourth quarter of 2018.

93. Upon information and belief, following approval of Bayer's BLA, BAY 94 will be indicated for overlapping patient population as Adynovate® and will, therefore, compete with

Baxalta's Adynovate® product, especially because BAY 94 and Adynovate® are both extended half-life pegylated Factor VIII products. Upon information and belief, Defendants are aware that BAY 94 will compete with Adynovate® for new patients.

94. Baxalta Inc. and Baxalta US have a strong interest in maintaining the market position of Adynovate®. Upon information and belief, Baxalta Inc. characterizes Adynovate® as a "blockbuster" treatment, which has been predicted to exceed $1 billion in sales by 2020.

95. Nektar has a strong interest in maintaining the market position of Adynovate®. Upon information and belief, Nektar receives the following payments from Baxalta Inc. and Baxalta US under their exclusive licensing agreement: escalating royalties of between 4-6% on global net revenue of Adynovate® up to $1.2 billion in revenue; a flat 13% royalty for revenue above $1.2 billion; and additional tiered revenue milestone payments based upon global net revenue of Adynovate®.

96. Upon information and belief, as the exclusive licensees of the '749 patent, Baxalta Inc. and Baxalta US plan to seek a declaration that Bayer's BAY 94 will infringe the '749 patent before the FDA approves Bayer's BLA. Baxalta Inc. has a history of asserting its patents against competitors in the hemophilia A treatment market even before the competitor has completed submission of its BLA to the FDA. *See, e.g.*, Complaint, *Baxalta Inc. v. Genentech, Inc.*, No. 1:17-cv-00509 (D. Del. May 4, 2017) (ECF No. 1) (alleging infringement of U.S. Patent No. 7,033,590 based on "Defendants' current and/or imminent manufacture, use, sale, offer to sell within the United States, and/or importation into the United States of Defendants' humanized bispecific antibody that binds Factor IX/IXa and Factor X to treat hemophilia A."); *see also* Answer, *Baxalta Inc. v. Genentech, Inc.*, No. 1:17-cv-00509 (D. Del. June 30, 2017) (ECF No. 9) ("As of [the date of Baxalta Inc.'s complaint], Genentech had not completed filing its Biologics License Application ('BLA') for emicizumab with FDA").

97. Based on, *inter alia*: the exclusive right granted by Nektar to Baxalta Inc. and Baxalta US to enforce the '749 patent; the history of litigation between the parties over the rights to Factor VIII pegylation technology, both in the United States and abroad; Defendants' past refusals to resolve disputes over the right to Factor VIII pegylation technology; Bayer's publicly

known, extensive, and meaningful preparations to obtain FDA approval to manufacture, use, offer to sell, and/or sell BAY 94, including its clinical trials and recent BLA submission; Bayer's publicly known intention to launch BAY 94 immediately upon obtaining FDA approval; Baxalta Inc.'s practice of seeking declarations of infringement against its competitors in the hemophilia A treatment market even before they have completed their FDA submissions; Defendants' strong interest in maintaining their position in the Factor VIII replacement therapy market, including Defendants' collaboration to develop, manufacture, and/or market Adynovate® and Defendants' financial interest in maintaining Adynovate's® market position, there is a real, immediate, and substantial controversy between the parties that warrants a declaratory judgment.

98. Upon information and belief, Defendants imminently intend to seek a declaratory judgment that BAY 94 will infringe the '749 patent.

99. The imminent threat of a challenge to Bayer's BAY 94 has cast uncertainty over the commercialization of BAY 94 and created a justiciable controversy.

THE '749 PATENT

100. The '749 patent, titled "Polymer-Factor VIII Moiety Conjugates," states on its face that it issued on December 28, 2010.

101. The '749 patent lists on its face the following inventors: Mary J. Bossard, Michael D. Bentley, and Ping Zhang.

102. The '749 patent lists on its face Nektar Therapeutics as the assignee.

103. The '749 patent states on its face that it issued from Application No. 11/702,302, a continuation of the '956 Application filed on February 26, 2004, which claims the benefit of priority to the original Provisional Application filed on February 26, 2003.

104. The '749 patent contains one independent claim and eighteen (18) dependent claims, which all depend on claim 1.

105. Independent claim 1 of the '749 patent recites:

> 1. A conjugate comprising a Factor VIII polypeptide covalently attached to one, two, three or four water-soluble polymers via a degradable 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, and

(ii) the water-soluble polymer is selected from the group consisting of poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, and poly(acryloylmorpholine).

COUNT 1: DECLARATORY JUDGMENT OF NON-INFRINGEMENT OF THE '749 PATENT

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

107. There is a real, immediate, substantial, and justiciable controversy between Bayer and Defendants concerning, *inter alia*, infringement of the '749 patent.

108. This controversy is amenable to specific relief through a decree of a conclusive character.

109. The manufacture, use, offer for sale, sale, and/or import of BAY 94 has not infringed and will not infringe, literally or under the doctrine of equivalents, by inducement or contributorily, any valid claim of the '749 patent.

110. For example, BAY 94 does not satisfy at least the following element of independent claim 1 of the '749 patent: "a Factor VIII polypeptide covalently attached to one, two, three or four water-soluble polymers via a degradable linkage." Ex. 1 at col.73 ll.2-4. This element is required by every claim of the '749 patent because claims 2-19 all depend on claim 1.

111. BAY 94 is pegylated via a thioether linkage to a cysteine residue. Ex. 2 at 271; Ex. 4 at 82. The '749 patent specification states that a thioether linkage is a "hydrolytically stable linkage," which is not a "degradable linkage" as required by the claims. *See* Ex. 1 at col.15 ll.50-55.

112. Therefore, BAY 94 has not infringed and will not infringe any valid claim of the '749 patent.

COUNT 2: DECLARATORY JUDGMENT OF INVALIDITY OF THE '749 PATENT

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

114. There is a real, immediate, substantial, and justiciable controversy between Bayer and Nektar concerning, *inter alia*, the invalidity of the claims of the '749 patent.

115. This controversy is amenable to specific relief through a decree of a conclusive character.

116. All claims of the '749 patent are invalid for failure to satisfy one or more of the requirements for patentability pursuant to 35 U.S.C. §§ 100 *et seq.*, including but not limited to §§ 102, 103, and/or 112.

117. Claims 1-19 of the '749 patent are invalid under § 102(a) because the claimed invention was known or used by others in this country, and/or was patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicants of the '749 patent. Each and every element of each and every claim of the '749 patent was disclosed in the prior art, including but not limited to, for example, U.S. Patent No. 6,048,720 to Dalborg et al. and/or one or more other prior art disclosures.

118. Claims 1-19 of the '749 patent are invalid under § 102(b) because the claimed invention was patented and/or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for the '749 patent in the United States. Each and every element of each and every claim of the '749 patent was disclosed in the prior art, including but not limited to, for example, U.S. Patent No. 6,048,720 to Dalborg et al. and/or one or more other prior art disclosures.

119. Claims 1-19 of the '749 patent are invalid under § 102(f) because the named inventors did not invent the subject matter of the '749 patent, but instead derived it from Bayer before the earliest claimed priority date of the '749 patent.

120. Claims 1-19 of the '749 patent are invalid under § 102(g) because the claimed invention was made in this country by another inventor who had not abandoned, suppressed, or

concealed it before the named inventors allegedly invented the subject matter of the '749 patent. As described above, Bayer conceived and reduced to practice the subject matter of the '749 patent in the 1990s and continued its research and development thereof to perfect its invention through the early 2000s until filing its own patent application(s) and BLA.

121. Claims 1-19 of the '749 patent are invalid under § 103(a) because the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which such subject matter pertains. Each and every element of each and every claim of the '749 patent was disclosed in prior art, derived from Bayer, and/or made in this country by another inventor who had not abandoned, suppressed, or concealed it before the earliest possible priority date of the '749 patent, including, but not limited to, for example, U.S. Patent No. 6,048,720 to Dalborg et al. and/or one or more other prior art disclosures. As of the earliest priority date of the '749 patent, a person of ordinary skill in the art would have been motivated to combine U.S. Patent No. 6,048,720 to Dalborg et al. with one or more other prior art disclosures and/or the knowledge of a skilled artisan to achieve the alleged invention and would have had a reasonable expectation of success in doing so.

122. Claims 1-19 of the '749 patent are invalid under § 112 because the specification is not enabling as of its earliest claimed priority date and does not teach those of ordinary skill how to make and use the full scope of the claimed invention without undue experimentation. For example, to the extent that Defendants deny non-infringement of BAY 94, then claims 1-19 are not enabled because BAY 94 does not include a "Factor VIII polypeptide" as that term is set forth in the '749 patent specification.

123. Claims 1-19 of the '749 patent are invalid under § 112 because, when read in light of the specification and prosecution history, the claims fail to inform those skilled in the art of the full scope of the invention with reasonable certainty. For example, to the extent that Defendants deny non-infringement of BAY 94, then claims 1-19 are indefinite because BAY 94 does not include a "Factor VIII polypeptide" as that term is set forth in the '749 patent specification.

124. Claims 1-19 of the '749 patent are invalid under § 112 because the specification does not convey to a person of ordinary skill that the inventors had possession of the claimed invention as of the earliest claimed priority date. For example, to the extent that Defendants deny non-infringement of BAY 94, then claims 1-19 are not adequately described because BAY 94 does not include a "Factor VIII polypeptide" as that term is set forth in the '749 patent specification.

125. Bayer is entitled to a judicial declaration that all claims of the '749 patent are invalid.

PRAYER FOR RELIEF

WHEREFORE, Bayer requests that the Court enter judgment in its favor and against Defendant Nektar as follows:

A. Declare that the manufacture, use, offer for sale, sale, and/or import of Bayer's BAY 94 product has not infringed and will not infringe, literally or under the doctrine of equivalents, by inducement or contributorily, any valid claim of the '749 patent;

B. Declare that claims 1-19 of the '749 patent are invalid;

C. Award Bayer its costs and reasonable attorney's fees to the extent permitted by law; and

D. Award Bayer such other and further relief as the Court deems just and proper.

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: August 30, 2017

SIDLEY AUSTIN LLP

/s/ *Sona De*

Bradford. J. Badke (*pro hac forthcoming*)
jbadke@sidley.com
Sona De (SBN# 193896)
sde@sidley.com
787 Seventh Avenue
New York, NY 10019
Telephone: (212) 839-5300
Facsimile: (212) 839-5599

Sue Wang (SBN# 286247)
555 California Street, Suite 2000
San Francisco, CA 94104
sue.wang@sidley.com
Telephone: (415) 772-1200
Facsimile: (415) 772-7400

Attorneys for Bayer HealthCare LLC