**UNITED STATES DISTRICT COURT**
**DISTRICT OF NEW JERSEY**

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| AMGEN INC., and<br>AMGEN MANUFACTURING, LIMITED<br>Plaintiffs,<br><br>v.<br><br>TEVA BIOPHARMACEUTICALS USA, INC.,<br>TEVA PHARMACEUTICALS USA, INC., and<br>TEVA PHARMACEUTICAL INDUSTRIES LTD.,<br><br>Defendants. | Civil Action No. _____ |

## COMPLAINT

Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited, by and through their undersigned attorneys, for their Complaint against Defendants Teva Biopharmaceuticals USA, Inc.; Teva Pharmaceuticals USA, Inc.; and Teva Pharmaceutical Industries Ltd. (collectively, "Defendants" or "Teva"), hereby allege as follows:

## THE PARTIES

1. Amgen Inc. ("Amgen") is a corporation existing under the laws of the State of Delaware with its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320. Amgen discovers, develops, manufactures, and sells innovative therapeutic products based on advances in molecular biology, recombinant DNA technology, and chemistry.

2. Amgen Manufacturing, Limited ("AML") is a corporation existing under the laws of Bermuda with its principal place of business in Juncos, Puerto Rico. AML

manufactures and sells biologic medicines for human therapeutic uses.

3. Upon information and belief, Defendant Teva Biopharmaceuticals USA, Inc. ("Teva Biopharmaceuticals") is a corporation existing under the laws of the State of Delaware with a place of business at 9410 Key West Avenue, Rockville, Maryland 20850.

4. Upon information and belief, Defendant Teva Pharmaceuticals USA, Inc. ("Teva USA") is a corporation existing under the laws of the State of Delaware with a place of business at 1090 Horsham Road, North Wales, Pennsylvania 19454.

5. Upon information and belief, Defendant Teva Pharmaceutical Industries Ltd. ("Teva Ltd.") is a foreign corporation existing under the laws of the State of Israel with a place of business at 5 Basel St., Petach Tikva, Israel.

6. Upon information and belief, Teva Biopharmaceuticals and Teva USA are wholly-owned subsidiaries of Teva Ltd.

## NATURE OF THE ACTION

7. This is a declaratory judgment action for infringement of U.S. Patent No. 8,058,398 ("the '398 patent"). This action arises under the Declaratory Judgments Act, 28 U.S.C. §§ 2201 and 2202 and the Patent Laws of the United States, 35 U.S.C. §§ 100 *et seq*. The act of infringement relates to, *inter alia*, Teva's imminent launch of its Lonquex® (lipegfilgrastim) product.

## JURISDICTION AND VENUE

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

9. This Court may declare the rights and other legal relations of the parties pursuant to 28 U.S.C. §§ 2201 and 2202, because this is a case of actual controversy within the Court's jurisdiction.

10. This Court has personal jurisdiction over each of the Defendants by virtue of the facts that, *inter alia*, each Teva Biopharmaceuticals, Teva USA, and Teva Ltd. has committed, or aided, abetted, contributed to, and/or participated in the commission of, the tortious act of patent infringement that has led to foreseeable harm and injury to Plaintiffs. This Court has personal jurisdiction over each of the Defendants for the additional reasons set forth below and for other reasons that will be presented to the Court if jurisdiction is challenged.

11. Upon information and belief, Teva Biopharmaceuticals develops biopharmaceuticals for sale and use throughout the United States, including in this District. Upon information and belief, Teva Biopharmaceuticals participated in the development of lipegfilgrastim as an agent of Teva Ltd. and/or in its own capacity.

12. This Court has personal jurisdiction over Teva Biopharmaceuticals because, *inter alia*, it conducts business in New Jersey in concert with Teva USA and Teva Ltd.

13. Upon information and belief, Teva USA, in concert with Teva Biopharmaceuticals and Teva Ltd., researches, develops, manufactures, and distributes prescription drugs for sale and use throughout the United States, including in this District.

14. This Court has personal jurisdiction over Teva USA because, *inter alia*, it is registered to do business in the State of New Jersey and derives substantial revenue

from operations in this District. In addition, Teva USA has engaged in substantial and continuing contacts with New Jersey. Upon information and belief, Teva USA employs more than 300 people in New Jersey at facilities in Fairfield Township and the Boroughs of Woodcliff Lake and Northvale. Additionally, Teva USA has recently been sued in this District and has consented to the personal jurisdiction of this Court. *See, e.g., Janssen Products, L.P. v. Teva Pharmaceuticals USA, Inc.*, Civil Action No. 12-03569, D.I. 8 (D.N.J. July 12, 2012); *Merck Sharp & Dohme Pharmaceuticals, SRL v. Teva Pharmaceuticals USA, Inc.*, Civil Action No. 07-1596, D.I. 23 (D.N.J. Aug. 17, 2007). Teva USA has further availed itself of the jurisdiction of this Court by asserting claims and counterclaims arising under the Patent Laws of the United States in other civil actions initiated in this jurisdiction. *See, e.g., Teva Pharmaceuticals USA, Inc. v. Sandoz Inc.*, Civil Action No. 12-2494, D.I. 1 (D.N.J. Apr. 26, 2012); *Teva Pharmaceuticals USA, Inc. v. Apotex, Inc.*, Civil Action No. 07-5514, D.I. 1 (D.N.J. Nov. 15, 2007).

15. Upon information and belief, Teva Ltd., by itself and/or through its wholly-owned subsidiaries, Teva Biopharmaceuticals and Teva USA, researches, develops, manufactures, and distributes numerous generic and proprietary-branded drugs for sale and use throughout the United States, including in this District.

16. This Court has personal jurisdiction over Teva Ltd. because, *inter alia*, it conducts business in New Jersey by and through its subsidiaries and derives substantial revenue from business transacted in New Jersey. Additionally, Teva Ltd. has recently consented to the personal jurisdiction of this Court. *See, e.g., Janssen Products, L.P. v. Teva Pharmaceuticals USA, Inc.*, Civil Action No. 12-03569, D.I. 8 (D.N.J. July 12,

2012); *Merck Sharp & Dohme Pharmaceuticals, SRL v. Teva Pharm. Indus. Ltd.*, Civil Action No. 07-1596, D.I. 23 (D.N.J. Aug. 17, 2007). Teva Ltd. has further availed itself of the jurisdiction of this Court by asserting claims arising under the Patent Laws of the United States in other civil actions initiated in this jurisdiction. *See, e.g., Teva Pharm. Indus. Ltd. v. Sandoz Inc.,* Civil Action No. 12-2494, D.I. 1 (D.N.J. Apr. 26, 2012); *Teva Pharm. Indus. Ltd. v. Apotex, Inc.*, Civil Action No. 07-5514, D.I. 1 (D.N.J. Nov. 15, 2007).

17. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(b), (c), and (d), and 1400(b).

**PATENT-IN-SUIT**

18. Amgen owns all rights, title, and interest in the '398 patent, which is directed to, *inter alia,* modified human granulocyte colony-stimulating factor ("G-CSF") polypeptides that selectively stimulate the production of neutrophils.

19. Amgen granted AML an exclusive license to the '398 patent.

20. The '398 patent is titled "Modified G-CSF Polypeptide" and was duly and legally issued by the United States Patent and Trademark Office ("USPTO") on November 15, 2011. A true and correct copy of the '398 patent is attached as Exhibit A.

21. The '398 patent claims priority to U.S. Patent Application No. 08/010,099, which was filed on January 28, 1993 and ultimately issued as U.S. Patent No. 5,581,476.

## DR. OSSLUND'S INVENTIONS

22. The '398 patent describes and claims an invention of an Amgen scientist, Dr. Timothy D. Osslund, relating to modified human G-CSF polypeptides. Dr. Osslund assigned to Amgen all rights and interest in the inventions claimed in the '398 patent.

23. Polypeptides, including G-CSF, are comprised of amino acids that are linked together in a chain-like fashion. Polypeptide chains have a three-dimensional shape, which may contain distinct, localized structures such as "α-helices," "β-sheets," "β-hairpins," and "loops." Natural forms of G-CSF are produced by animals (including humans) and stimulate the production of neutrophils, a type of white blood cell.

24. In the modified human G-CSF polypeptides claimed in the '398 patent, a polysaccharide is directly attached to an external loop in the human G-CSF polypeptide, and another molecule, called polyethylene glycol ("PEG"), is attached to the polysaccharide. The resulting modified human G-CSF polypeptide has the ability to selectively stimulate the production of neutrophils.

## AMGEN'S FDA-APPROVED G-CSF-BASED PRODUCTS AND TEVA'S FDA-APPROVED G-CSF-BASED PRODUCT

25. Amgen has secured U.S. Food and Drug Administration ("FDA") approval for two G-CSF products. Amgen first received FDA-approval in 1991 for NEUPOGEN® (filgrastim), Biologics Licensing Application ("BLA") No. 103353, for decreasing the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever. The FDA's approval of NEUPOGEN®

(filgrastim) was based on a full complement of pre-clinical and clinical trials, including two successful Phase III pivotal trials. At that time, NEUPOGEN® (filgrastim) was the first and only biologic product approved to decrease the incidence of infection in cancer patients receiving chemotherapy, and Amgen received the 1991 UK Prix Galien medal for its ground-breaking, innovative work in bringing this important biomedical advance to patients. After Amgen conducted further clinical testing, the FDA later approved several additional indications for the therapeutic use of NEUPOGEN® (filgrastim), including the treatment of patients with severe chronic neutropenia, patients with acute myeloid leukemia receiving induction or consolidation chemotherapy, patients receiving bone marrow transplant, and patients undergoing peripheral blood progenitor cell collection and therapy.

26. The active ingredient in NEUPOGEN® is filgrastim, a recombinantly-expressed, 175-amino acid form of G-CSF known as recombinant methionyl human granulocyte-colony stimulating factor. By binding to specific receptors on the surface of certain types of cells, NEUPOGEN® (filgrastim) stimulates the production of neutrophils. In the human body, NEUPOGEN® (filgrastim) has an elimination half-life of 3.5 hours. For cancer patients receiving myelosuppressive chemotherapy, NEUPOGEN®'s (filgrastim) half-life necessitates that it be administered on a daily basis until the patient's absolute neutrophil count exceeds 10,000/$mm^3$, which may require daily administration for up to two weeks. From a clinical perspective, this means that patients can either (i) return to the doctor's office daily for up to two weeks after the administration of a cytotoxic chemotherapy cycle to receive their full dosing regimen of NEUPOGEN®

(filgrastim); or (ii) self-inject NEUPOGEN® (filgrastim) on a daily basis to complete the multi-day dosing schedule. Because NEUPOGEN® (filgrastim) is administered on a daily basis, it is sometimes referred to as a "short-acting" G-CSF therapeutic.

27. On information and belief, Teva will launch its own "short acting" G-CSF product called "GRANIX™" or "tbo-filgrastim" in the United States in 2013. GRANIX™ has the same amino acid sequence as NEUPOGEN® (filgrastim), and has been marketed in Europe as "Tevagrastim®" since 2008. In the United States, GRANIX™ is approved to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. The FDA's approval of GRANIX™ was based on a Phase III clinical trial establishing that GRANIX™ was superior to placebo and non-inferior to Amgen's filgrastim.

28. Amgen also holds FDA-approved BLA No. 125031 for a modified G-CSF, which is sold under the brand name Neulasta® (pegfilgrastim). The active ingredient in Neulasta® is pegfilgrastim, a 175-amino acid form of filgrastim polypeptide that has a PEG molecule attached to the first amino acid (*i.e.*, methionine) of its polypeptide chain. Like NEUPOGEN® (filgrastim), Neulasta® (pegfilgrastim) stimulates the production of neutrophils by binding to specific cell surface receptors. However, Neulasta® (pegfilgrastim) remains in the body longer than NEUPOGEN® (filgrastim), enhancing the production of neutrophils. Neulasta® (pegfilgrastim) is administered once per chemotherapy cycle dosing, *i.e.*, patients can be treated with a single dose of Neulasta® (pegfilgrastim) rather than the multiple day dose of the filgrastim products.

Because Neulasta® (pegfilgrastim) may be administered once per chemotherapy cycle, it is sometimes referred to as a "long-acting" G-CSF therapeutic. Among the advantages that Neulasta® (pegfilgrastim) provides over NEUPOGEN® (filgrastim) is that the once-per-cycle dosing of Neulasta® (pegfilgrastim) reduces the burden on patients and doctors associated with daily dosing of NEUPOGEN® (filgrastim). Neulasta® (pegfilgrastim) is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

**TEVA'S IMMINENT INFRINGEMENT OF THE '398 PATENT**

29. Upon information and belief, Teva seeks to import, manufacture, use, distribute, sell, and/or offer to sell a product called "lipegfilgrastim" in the United States upon FDA approval and prior to the expiration of the '398 patent.

30. Teva describes its lipegfilgrastim product as "a long acting granulocyte colony-stimulating factor (G-CSF)" that is "being developed to reduce the duration of severe neutropenia in cancer patients undergoing chemotherapy." *See* "Teva Announces Successful Results of Phase III Study of Its Long-Acting G-CSF Product (Lipegfilgrastim) in Breast Cancer Patients," http://www.tevapharm.com/media/news/pages/2011/1580531.aspx?category=biosimilars/biologics (attached hereto as Exhibit B). Teva has given notice to Amgen and AML, and promoted to the world, that its lipegfilgrastim product has the ability to selectively stimulate the production of neutrophils. *See, e.g.*, O. Gladkov, *et al.*, "Efficacy and Safety of Lipegfilgrastim in Patients with Lung Cancer Who Are Receiving Chemotherapy," presented at the

MASCC/ISOO International Symposium on Supportive Care in Cancer, New York, New York, on June 28-30, 2012 (attached hereto as Exhibit C).

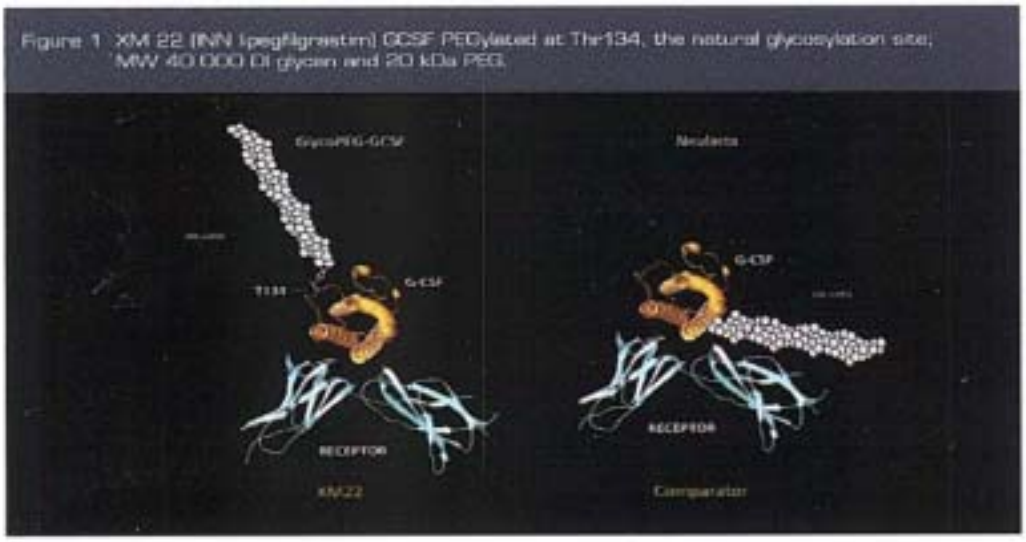
31. Teva refers to its long-acting, glyco-pegylated G-CSF as "lipegfilgrastim" "Lonquex," or "XM-22."

32. Upon information and belief, in connection with various medical and scientific conferences, Teva has given notice to Amgen and AML and promoted to the world that its lipegfilgrastim product contains a modified G-CSF polypeptide, wherein a polysaccharide is attached directly to an external loop of G-CSF, and PEG is attached to the polysaccharide. *See, e.g.*, I. Bondarenko, *et al*., "Efficacy and Safety of Lipegfilgrastim Compared with Pegfilgrastim in Patients with Breast Cancer Who Are Receiving Chemotherapy," 30 J. Clinical Oncology, e19587 (2012) (attached hereto as Exhibit D); E. Kohler, *et al.*, "Glyco-PEGylated R-metHuG-CSF (XM22/Lipegfilgrastim) – a Novel Long-Acting Once-per-cycle Filgrastim: Pharmacokinetics and Pharmacodynamics for Body Weight Adjusted Doses and a 6mg Fixed Dose in Healthy Volunteers," 47 Eur. J. Cancer, S149 (2011) ("the Kohler Presentation") (attached hereto as Exhibit E).

33. Upon information and belief, at various medical and scientific conferences, as well as through Phase III clinical trial data released by Teva, Teva has actively promoted its lipegfilgrastim product to the medical community and the world, stating, *inter alia*, that "[t]he product is designed to provide clinical efficacy and safety profiles which are fully comparable to Neulasta™ (sic)." *See* Exhibit B.

34. In the Kohler Presentation, which featured named presenters from three

separate Teva entities – BioGenerix, Teva Biopharmaceuticals Development, and Teva Biopharmaceuticals USA – the presenters highlighted and promoted Teva's lipegfilgrastim product (identified as "XM22" on the left ) as being similar to and a competitor to Amgen's Neulasta® product (identified as "Comparator" on the right) in Figure 1 of their poster:




35. The lipegfilgrastim product that Teva seeks to market in the United States has proceeded through pre-clinical and clinical testing, and is the subject of submissions for regulatory approval in the United States.

36. Upon information and belief, lipegfilgrastim (referred to as "GlycoPEG-GCSF") was the subject of Phase I clinical trials that were initiated in November 2006 and March 2007 by Neose Technologies, Inc. ("Neose"). Upon information and belief, data from Phase I clinical trials of lipegfilgrastim were announced in November 2007.

37. Upon information and belief, Neose and its co-development partner, BioGeneriX AG, a subsidiary of ratiopharm GmbH ("ratiopharm"), advanced

lipegfilgrastim to Phase II clinical trials in 2008. Upon information and belief, Neose was subsequently dissolved.

38. Upon information and belief, in August 10, 2010, Teva announced that it had completed an acquisition of ratiopharm. Upon information and belief, through this acquisition, lipegfilgrastim was added to Teva's portfolio.

39. Upon information and belief, Teva announced data from a single successful Phase III clinical trial involving the treatment of patients suffering from breast cancer with lipegfilgrastim on June 6, 2011.

40. Upon information and belief, a second Phase III clinical trial with lipegfilgrastim was also completed in patients suffering from non-small cell lung cancer. Upon information and belief, in this study, lipegfilgrastim failed to achieve a statistically significant decrease in the incidence of febrile neutropenia as compared to placebo, and thereby failed to meet the primary endpoint of the trial.

41. During a December 11, 2012 investor meeting that was advertised on the homepage of its company website, Teva provided public notice to Amgen, AML, and the world that it had filed a BLA with the FDA in December 2012, seeking approval to market and sell its glycol-pegylated G-CSF product in the United States. *See, e.g.*, December 11, 2012 "Teva Pharmaceutical Industries Ltd Analyst Meeting Presentation," at Slide 153, http://ir.tevapharm.com/phoenix.zhtml?c=73925&p=irol-EventDetails&EventId=4878396 (attached hereto as Exhibit F).

42. During the same December 11, 2012 investor meeting, Teva further stated that it intends to launch a long-acting G-CSF in the United States in 2014. *See id*. at

Slide 182.

43. By filing a BLA for its lipegfilgrastim product with the FDA, Teva has represented to the FDA that it has completed sufficient clinical testing and analysis of its lipegfilgrastim product to obtain FDA approval to manufacture, offer for sale, sell, and distribute its lipegfilgrastim product in the United States.

44. On information and belief, the FDA has formally accepted Teva's BLA for its lipegfilgrastim product for review.

45. At least one prominent foreign regulatory agency has already found that Teva's regulatory submissions and data support approval of lipegfilgrastim. On August 8, 2013, Teva issued a press release and announced to Amgen, AML, its investors, and the world that the European Medicines Agency ("EMA") had granted a Marketing Authorization in the European Union for Lonquex® for the reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy, with the exception of chronic myeloid leukemia and myelodysplastic syndromes. *See* "Teva Receives European Marketing Authorization for Lonquex® (XM22 lipegfilgrastim)," http://www.tevapharm.com/ Media/News/Pages/ 2013/1846232.aspx (attached hereto as Exhibit G). Upon information and belief, the Marketing Authorization granted by the EMA allows Teva to begin marketing and selling lipegfilgrastim for certain human therapeutic uses in Europe. *Id*.

46. In this same press release, Dr. Rob Koremans, President and CEO of Teva Specialty Medicines, stated that "Lonquex® is an alternative G-CSF treatment for helping manage neutropenia during myelosuppressive chemotherapy. The European approval

comes earlier than expected, just 8 weeks after the positive CHMP opinion. We look forward to providing this oncology supportive care treatment option in all European Union member states." In addition, Dr. Michael Hayden, Teva's President of Global Research and Development and Chief Scientific Officer stated that "[t]his approval is testament to Teva's commitment to bringing new and alternative treatments to market to support clinicians in caring for patients." *Id*.

47. Pursuant to the Prescription Drug User Fee Act V (21 U.S.C. § 301 *et seq.*; "PDUFA V"), which sets deadlines for the FDA's review of BLA applications filed on or after October 1, 2012, the FDA seeks to complete its final review of BLA applications within ten months of the day that the FDA accepts an application for filing. PDUFA V further specifies that the FDA may accept a BLA application for filing within 60 days of the application's filing date. As Teva filed its BLA for its lipegfilgrastim product in early December 2012, Amgen reasonably believes that Teva's BLA will receive FDA approval as early as December 2013, well in advance of the expiration of the '398 patent.

48. Upon information and belief, Teva has made and continues to make additional meaningful preparations to import, use, distribute, sell, and/or offer to sell its lipegfilgrastim product in the United States upon the FDA approval of its BLA without a license to or authorization under Amgen's '398 patent. On information and belief, Teva's meaningful preparations include:

a. hiring key management and sales personnel to market and sell lipegfilgrastim in the United States;

b. retaining outside consultants and vendors to assist in its marketing

and sale of lipegfilgrastim in the United States; and

c. conducting market research and customer interviews regarding the utilization of and bases for choosing between NEUPOGEN® (filgrastim) and Neulasta® (pegfilgrastim).

49. Upon information and belief, Teva's modified G-CSF polypeptide as embodied by its lipegfilgrastim product will infringe one or more claims of the '398 patent.

50. Upon information and belief, Teva's infringement of the '398 patent will be willful and deliberate.

51. As a direct and proximate consequence of the planned and intended infringement by Teva, Amgen will be injured in its business and property rights unless the infringement is enjoined by the Court, and will suffer injury and damages for which it is entitled to relief.

**FIRST CAUSE OF ACTION**
**(Declaratory Judgment of Infringement of the '398 Patent)**

52. Amgen and AML re-allege and incorporate by reference the allegations in Paragraphs 1 through 51 above.

53. Amgen and AML seek a judicial determination and declaration that Teva will directly infringe, either literally or under the doctrine of equivalents, and/or induce infringement of one or more claims of the '398 patent under 35 U.S.C. §§ 271(a) and/or (b) by making, importing, using, selling, and/or offering for sale in the United States products containing lipegfilgrastim.

## PRAYER FOR RELIEF

WHEREFORE, Amgen and AML request that the Court enter judgment in their favor and against Teva as follows:

(1) Declaring that Teva will infringe one or more claims of the '398 patent;

(2) Declaring that Teva's infringement will be willful and that this is an exceptional case under 35 U.S.C. § 285;

(3) Preliminarily and permanently enjoining Teva, their respective officers, agents, servants and employees, and those persons in active concert or participation with any of them, from infringing the '398 patent;

(4) Awarding Amgen and AML their attorneys' fees, costs, and expenses; and

(5) Awarding Amgen and AML such other and further relief as this Court may deem to be just and proper.

Dated: August 14, 2013

s/ Michael R. Griffinger

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