UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BRISTOL-MYERS SQUIBB CO., E. R. SQUIBB & SONS L.L.C., ONO PHARMACEUTICAL CO., LTD., and TASUKU HONJO,	)	
Plaintiffs,	)	C.A. No. _____
v.	)	**JURY TRIAL DEMANDED**
GENENTECH, INC.,	)	
Defendant.	)	

COMPLAINT

Plaintiffs Bristol-Myers Squibb Co. ("BMS"), E. R. Squibb & Sons L.L.C. ("Squibb"), Ono Pharmaceutical Co., Ltd. ("Ono"), and Tasuku Honjo (collectively "Plaintiffs"), for their complaint for patent infringement against Defendant Genentech, Inc. ("Defendant" or "Genentech"), hereby allege as follows:

INTRODUCTION

1. According to the American Cancer Society, more than one million people in the United States are diagnosed with cancer each year (http://www.cancer.org/cancer/index). Cancer is a disease that results from the uncontrolled proliferation of cells that were once normal but have transformed into cancerous cells. Although the human immune system sometimes has the potential to eliminate cancerous cells, cancer cells have the ability to "turn off" or evade the immune system, allowing the cancer cells to grow unchecked. Tumor growth and tumor metastasis can lead to devastating disease, and possibly death. Cancer treatments are therefore developed to decrease tumor growth and metastasis.

2. This case relates to groundbreaking treatments for cancer that fall within a field known as "immunotherapy." The treatment of cancer using immunotherapy represents a scientific breakthrough that is revolutionizing cancer treatment by manipulating a patient's immune system to eliminate cancer cells.

3. The human immune system is formed of organs, specialized cells, and substances that protect individuals from infections and disease. T cells are one class of specialized cells that play an important role in the human immune system. One major function of T cells is to destroy pathogens or malignant cells, and to do that the T cell must distinguish healthy cells from pathogens or malignant cells through the activation or deactivation of various receptors on the T cell surface. One of the receptors that T cells carry on their surface is a protein called programmed death-1 receptor ("PD-1"). PD-1 functions as a checkpoint on the immune system that can downregulate T cell activity to prevent an overactive immune response. To activate its inhibitory function, PD-1 must bind to one of its ligands. Programmed death-ligand 1 ("PD-L1") is one of these ligands.

4. Numerous forms of cancers express PD-L1 on their cell surface, and can therefore exploit PD-1's ability to downregulate the immune response. When PD-L1, such as that expressed on a cancer cell, binds to PD-1 on immune cells, such as a T cell, it can result in the suppression of T cell migration, proliferation and secretion of cytotoxic mediators, which in turn will eliminate or decrease an anticancer immune response. In other words, cancer cells expressing PD-L1 can activate the PD-1 checkpoint to prevent a patient's immune system from destroying cancer cells.

5. The inventions at issue here generally relate to treatments for cancer and enhancing immune responses by administering antibodies that bind to PD-L1 ("anti-PD-L1

antibodies"). Types of anti-PD-L1 antibodies are shown by the inventions to inhibit the interaction between PD-1 and PD-L1. By binding to PD-L1 and blocking its interaction with PD-1, the anti-PD-L1 antibodies act as checkpoint inhibitors that release the brakes on the immune system, freeing the immune cells to recognize, attack and destroy cancer cells.

6. On information and belief, Genentech knows or should have knowledge of Plaintiffs' inventions. In its U.S. Patent Application No. 14/726,329, filed on July 11, 2014 and titled "Anti-PD-L1 Antibodies and Diagnostic Uses Thereof," Genentech describes and has claims that include limitations directed to Plaintiffs' anti-PD-1 antibody nivolumab and anti-PD-L1 antibody MDX-1105.

7. Genentech is exploiting Plaintiffs' inventions with its later-developed antibody product TECENTRIQ (atezolizumab), an anti-PD-L1 antibody used in methods for treating cancer and for enhancing an immune response.

8. Plaintiffs and Genentech are competitors in the field of immunotherapy.

9. The Plaintiffs also invented antibodies that bind to PD-1 ("anti-PD-1 antibodies"), and put this scientific breakthrough into practice by developing an anti-PD-1 antibody called OPDIVO (nivolumab), the first anti-PD-1 antibody approved anywhere in the world for cancer treatment, and the first anti-PD-1 antibody approved in the United States for the treatment of lung cancer.

10. Nivolumab is a monoclonal antibody that recognizes and binds to PD-1. When nivolumab binds to PD-1, it prevents PD-1 from binding its ligands. Using nivolumab to block the interaction between PD-1 and its ligands enhances the T cell response generated by the patient's immune system.

11. Clinical testing of nivolumab confirmed the remarkable promise of checkpoint inhibitors as targets for immunotherapy. After rigorous worldwide testing, on July 4, 2014, nivolumab became the first anti-PD-1 antibody approved anywhere in the world for treating cancer, when Japanese regulatory authorities approved nivolumab for the treatment of melanoma, a deadly form of skin cancer (http://www.ono.co.jp/eng/news/pdf/sm_cn140704.pdf). On December 22, 2014, the FDA approved nivolumab for treatment of advanced melanoma in the United States.

12. Plaintiffs have continued worldwide development of nivolumab for treatment of a broad range of cancers, including non-small cell lung cancer, renal cell carcinoma, head and neck cancer, glioblastoma, and non-Hodgkin lymphoma. In Phase III clinical testing for lung cancer, patients with advanced lung cancer who received nivolumab showed superior overall survival (41% reduction in the risk of death) compared to those who received the standard of care chemotherapy agent docetaxol (http://news.bms.com/press-release/fda-approves-opdivo-nivolumab-treatment-patients-previously-treated-metastatic-squamou). Based, at least in part, on these clinical results, on February 27, 2015, the FDA accepted Plaintiffs' Biologics License Application ("BLA") for use of nivolumab to treat lung cancer. Just days later, on March 4, 2015, the FDA approved nivolumab for treatment of advanced non-small cell lung cancer in the United States. On November, 23, 2015, the FDA approved nivolumab for the treatment of patients with advanced renal cell carcinoma, a form of kidney cancer. These clinical results and the FDA's recent approval of nivolumab for the treatment of various additional forms of cancer confirm that the cancer treatments developed by the Plaintiffs can be used to save the lives of patients suffering from cancer.

PARTIES

13. BMS is a corporation organized under the laws of the state of Delaware, with a principal place of business at 345 Park Ave., New York, New York 10154. E. R. Squibb & Sons L.L.C., is a limited liability company organized and existing under the laws of the state of Delaware, with its principal place of business at Route 206 & Province Line Road, Princeton, New Jersey 08543. Ono is a corporation organized under the laws of Japan, with a place of business at 8-2 Kyutaromachi 1-chome, Chuo-ku, Osaka 541-8564, Japan. Tasuku Honjo is an individual with a place of business at Kyoto University, Graduate School of Medicine, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan.

14. On information and belief, Defendant Genentech, Inc. is a wholly-owned subsidiary of Roche Holdings, Inc. and is a corporation organized under the laws of the state of Delaware, with its principal place of business at 1 DNA Way, South San Francisco, California 94080. Genentech is in the business of manufacturing, marketing, distributing, offering for sale, and selling biologic drug products that are distributed and sold throughout the United States, including in Delaware.

15. Genentech is a biotechnology company that develops, manufactures and commercializes medicines to treat patients. On information and belief, Genentech relies on and actively seeks patent protection for its medicines. On information and belief, Genentech regularly enforces its patent and other intellectual property rights, and has been named as a defendant in multiple patent litigations.

JURISDICTION AND VENUE

16. This is an action for patent infringement arising under the Patent Laws of the United States, 35 U.S.C. § 271 et seq., including an action seeking a declaratory judgment pursuant to 28 U.S.C. §§ 2201-2202.

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

18. This Court has personal jurisdiction over Genentech because it is incorporated in Delaware and registered with the Delaware Department of State to transact business in Delaware and, upon information and belief, Genentech has systematic and continuous contacts in Delaware, regularly transacts business in Delaware, has derived substantial revenue from sales of pharmaceutical products in Delaware, and markets its anti-PD-L1 antibody atezolizumab in Delaware. On information and belief, Genentech has consented to jurisdiction in Delaware in one or more prior cases arising out of its manufacture, use, offer for sale, sale and/or importation of pharmaceutical products, including cases Genentech initiated as the plaintiff.

19. Defendant resides in this judicial district and venue is proper in this district under 28 U.S.C. § 1400(b).

THE PATENT-IN-SUIT

20. On August 2, 2016, the United States Patent & Trademark Office ("USPTO") duly and legally issued U.S. Patent No. 9,402,899 ("the '899 patent") titled "Immunopotentiative Composition." A true and correct copy of the '899 patent is attached hereto as Exhibit 1. The inventors of the '899 patent showed for the first time that anti-PD-L1 antibodies were useful in methods to treat cancer. Dr. Tasuku Honjo is a co-inventor and original co-assignee of the '899 patent. Ono is an original co-assignee and exclusive licensor of BMS under the '899 patent.

BMS and Squibb are each exclusive licensees of one or more exclusionary rights under the '899 patent.

21. The '899 patent issued from a divisional application of U.S. Application No. 12/959,307, filed on December 2, 2010 (now U.S. Pat. No. 8,728,474), which is a divisional application of U.S. Application No. 12/538,698, filed on August 10, 2009 (now U.S. Pat. No. 8,168,179), which is a divisional application of U.S. Application No. 10/519,925, filed on January 3, 2005 (now U.S. Pat. No. 7,595,048), which is a National Stage Entry of PCT/JP03/08420 filed on July 2, 2003, which claims priority based on Japanese Patent Application Nos. 2002-194491 and 2003-029846 filed on July 3, 2002 and February 6, 2003, respectively.

22. The claims of the '899 patent are generally directed to methods of treating cancer by administering an anti-PD-L1 monoclonal antibody that inhibits the interaction between PD-1 and PD-L1. By way of example, claim 1 of the '899 patent is:

> A method of treating a tumor in a human patient in need thereof comprising administering to the human an effective amount of an anti-PD-L1 monoclonal antibody that inhibits an interaction between PD-1 and PD-L1, wherein the anti-PD-L1 monoclonal antibody treats the tumor in the patient.

GENENTECH'S TECENTRIQ PRODUCT

23. On information and belief, Genentech is marketing, manufacturing, distributing, using, offering for sale, selling, and/or importing TECENTRIQ in the United States. According to its prescribing information, TECENTRIQ is a PD-L1 blocking antibody that is indicated for treating patients with types of cancer.

24. As shown by prescribing information for TECENTRIQ, Genentech received approval from the FDA on May 18, 2016 to market and sell TECENTRIQ as a treatment for

certain patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within twelve months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. Genentech received approval from the FDA on October 18, 2016 to market TECENTRIQ as a treatment for patients with metastatic non-small cell lung cancer ("NSCLC") who have disease progression during or following platinum-containing chemotherapy. TECENTRIQ is administered in a 1200 milligram dose as an intravenous infusion over 60 minutes every 3 weeks.

25. The active ingredient in Genentech's TECENTRIQ product is the anti-PD-L1 antibody atezolizumab. As stated in the TECENTRIQ prescribing information, atezolizumab is a humanized IgG1 monoclonal antibody that binds to human PD-L1, thereby inhibiting the interaction of PD-L1 with PD-1. Atezolizumab interferes with the PD-L1/PD-1 mediated inhibition of the immune response in order to produce an anti-tumor immune response.

The Use of TECENTRIQ Infringes the '899 Patent

26. On information and belief, Genentech is currently manufacturing, distributing, using, offering for sale, selling, and/or importing in the United States its TECENTRIQ antibody product to be prescribed and used for the treatment of cancer according to the TECENTRIQ prescribing information.

27. As described above, TECENTRIQ is used for treating a tumor in a human patient. TECENTRIQ is administered in an effective amount. The TECENTRIQ antibody (atezolizumab) is an anti-PD-L1 monoclonal antibody that inhibits an interaction between PD-1 and PD-L1. When administered to a human patient with a tumor, the TECENTRIQ antibody treats the tumor in the patient.

28. On information and belief, TECENTRIQ has been and is currently being used according to the prescribing information. The use of TECENTRIQ according to the prescribing information infringes at least claim 1 of the ’899 patent.

29. As described above, the prescribing information for TECENTRIQ describes atezolizumab as a humanized antibody. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 2, 20, and 43 of the ’899 patent.

30. TECENTRIQ has been approved to treat types of cancers, as described above, including solid tumors. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 3, 21, and 37 of the ’899 patent.

31. On information and belief, the administration of TECENTRIQ to patients is used to decrease tumor growth. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 4 and 19 of the ’899 patent.

32. On information and belief, the administration of TECENTRIQ to patients is used to suppress tumor metastasis. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 5, 22, and 36 of the ’899 patent.

33. TECENTRIQ has been approved to treat types of cancers, as described above, and those include types of urothelial carcinoma and non-small cell lung cancer. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 6-9, 12, 23-26, 29, 38-42, and 44-45 of the ’899 patent.

34. TECENTRIQ has been approved for administration by intravenous infusion. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 16 and 33 of the ’899 patent.

35. As described above, the prescribing information for TECENTRIQ describes atezolizumab as an IgG1 antibody. The use of TECENTRIQ according to the prescribing information therefore infringes at least claims 46-51 of the ’899 patent.

36. When medical professionals or others administer TECENTRIQ according to the prescribing information, they directly infringe the ’899 patent.

37. On information and belief, Genentech knows that TECENTRIQ has been and is currently being used according to the prescribing information.

38. On information and belief, Genentech’s antibody atezolizumab is described in U.S. Patent No. 8,217,149 (“the ’149 patent”), assigned to Genentech, Inc. and titled “Anti-PD-L1 Antibodies, Compositions and Articles of Manufacture.”

39. On information and belief, at least claims 1-3, 7-9, 13-17, 21 and 50-61 of the ’149 patent claim atezolizumab, the active ingredient in TECENTRIQ.

40. On information and belief, Genentech has known about the ’899 patent and has known that the use of TECENTRIQ to treat cancer infringes at least claims 1-9, 12, 16, 19-26, 29, 33, and 36-51 of the ’899 patent since at least approximately August 2, 2016 when the ’899 patent issued and, in any event, no later than upon receiving a copy of this complaint. In an information disclosure statement filed during the pendency of the application that led to the ’149 patent, Genentech cited multiple patents identifying Tasuku Honjo and his colleagues as inventors. In particular, Genentech cited to Honjo’s U.S. Patent No. 7,595,048 (“the ’048 patent”). As described above, the ’899 patent is a direct descendant of the ’048 patent. In addition, Genentech was mailed an International Search Report from the WIPO on April 29, 2010 in connection with its International Patent Application No. PCT/US2009/067104 (“the ’104 PCT”) that identified Honjo’s European Patent No. EP1537878 (“EP878 patent”) as a reference

of particular relevance in view of which Genentech's claimed inventions could not be considered novel or could not be considered to involve an inventive step when taken alone. The EP878 patent is a European counterpart to the '899 patent and discloses methods of treating tumors with anti-PD-L1 antibodies.

41. On information and belief, the '104 PCT covers Genentech's TECENTRIQ antibody product. On information and belief, by at least as early as about April 29, 2010, Genentech was aware of the Honjo patent family and was aware that the Honjo patent family included issued patents containing claims to methods of using anti-PD-L1 antibodies to treat tumors. On information and belief, Genentech knew or should have known that the use of TECENTRIQ in methods of treating a tumor would infringe claims in the Honjo patent family at least as early as about April 29, 2010.

42. Genentech's TECENTRIQ is especially made for use in infringing the '899 patent, and has no substantial non-infringing uses. By virtue of obtaining approval to market and sell TECENTRIQ as a treatment for certain patients with bladder cancer and lung cancer, Genentech has the specific intent to cause infringement of the '899 patent or, at a minimum, Genentech has been willfully blind to the infringement of the '899 patent that will inevitably result.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 9,402,899

43. Plaintiffs incorporate by reference paragraphs 1-42 as if fully set forth herein.

44. On information and belief, Genentech is marketing, making, using, selling, offering for sale, and/or importing atezolizumab in the United States for the treatment of cancer. On information and belief, atezolizumab is being used for the treatment of cancer in the United States. As set forth above, Genentech is thereby infringing at least claims 1-9, 12, 16, 19-26, 29,

33, and 36-51 of the ’899 patent, including by actively inducing infringement under 35 U.S.C. § 271(b) and as a contributory infringer under 35 U.S.C. § 271(c).

45. On information and belief, Genentech has been aware of the ’899 patent since at least approximately August 2, 2016, when the USPTO issued the ’899 patent and Genentech’s infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’899 patent.

46. Plaintiffs have been and will continue to be injured by and have been and will continue to suffer substantial damages as a result of Genentech’s infringement.

47. This case is exceptional and Plaintiffs are entitled to an award of attorneys’ fees under 35 U.S.C. § 285.

JURY DEMAND

Under Federal Rule of Civil Procedure 38, Plaintiffs demand trial by jury of all issues so triable.

PRAYER FOR RELIEF

Wherefore, Plaintiffs respectfully request the following relief:

(a) entry of a judgment that Defendant infringes and will infringe the ’899 patent;

(b) an award of damages sufficient to compensate Plaintiffs for infringement of the ’899 patent, together with pre- and post-judgment interest and costs as fixed by the Court as provided by 35 U.S.C. § 284;

(c) entry of an order compelling Defendant to compensate Plaintiffs for any ongoing or future infringement of the ’899 patent, in an amount and under terms appropriate for the circumstances;

(d) entry of an order that Defendant's infringement has been willful, and increased damages pursuant to 35 U.S.C. § 284;

(e) judgment that this is an exceptional case pursuant to 35 U.S.C. § 285 and an award to Plaintiffs of their reasonable attorney fees, costs, and expenses in this action pursuant to 35 U.S.C. § 285; and

(f) such other relief as the Court may deem just and proper.

Dated: July 26, 2017

Respectfully submitted,

FARNAN LLP

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