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. 14-cv-1131-GMS
v.	)	**JURY TRIAL DEMANDED**
MERCK & CO., INC. and MERCK SHARP & DOHME CORP.,	)	
Defendants.	)	

AMENDED 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 Defendants Merck & Co., Inc. and Merck Sharp & Dohme Corp. (collectively "Defendants" or "Merck"), 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 a human's natural immune system has the potential to eliminate cancerous cells, cancer cells have the ability to "turn off" the immune system thus allowing the cancer cells to continue to grow unchecked.

2. This case relates to a groundbreaking type of cancer treatment called "immunotherapy." Treating cancer using immunotherapy is a scientific breakthrough and has the

potential to revolutionize cancer treatment by using a patient's own immune system to eliminate cancer cells.

3. T cells are an important part of the human immune system. In addition to eliminating foreign matter such as bacteria and viruses from a human body, they also help remove cancerous cells in the body. T cells carry a protein called PD-1 on their surface. PD-1 serves as an immune system checkpoint, shutting down the T cells' activity at the appropriate time to prevent an overactive immune response. Cancer cells can exploit the PD-1 protein's ability to trigger the immune checkpoint. When the PD-1 is triggered in this way, it shuts down or decreases the T cells' activity of removing the unwanted cancer cells from the body. Thus, the triggering of the PD-1 checkpoint can prevent a patient's immune system from destroying the cancer cells.

4. The invention at issue here covers using antibodies that bind to PD-1 ("anti-PD-1 antibodies") in a method for treating cancer. By binding to PD-1 and blocking the PD-1 checkpoint pathway, the anti-PD-1 antibodies allow a patient's immune system to resume its ability to recognize, attack, and destroy cancer cells.

5. The plaintiffs put this scientific breakthrough into practice by developing an anti-PD-1 antibody called nivolumab, the first anti-PD-1 antibody approved anywhere in the world for cancer treatment.

6. Merck is threatening to exploit, and is exploiting, that invention with a later-developed anti-PD-1 antibody. As described below, Merck is preparing to infringe, and is infringing, plaintiffs' patent for methods of treating cancer with anti-PD-1 antibodies.

PARTIES

7. 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 541-8654, 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.

8. On information and belief, Defendant Merck & Co., Inc. is a corporation incorporated under the laws of the state of New Jersey with a place of business at 1 Merck Dr., Whitehouse Station, New Jersey, 08889. On information and belief, Defendant Merck Sharp & Dohme Corp. is a subsidiary of Merck & Co., Inc., and is a corporation incorporated under the laws of the state of New Jersey with a place of business at 1 Merck Dr., Whitehouse Station, New Jersey, 08889.

JURISDICTION AND VENUE

9. 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.

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

11. This Court has personal jurisdiction over both Defendants because they are registered with the Delaware Department of State to transact business in Delaware and, upon

information and belief, have systematic and continuous contacts in Delaware, do regularly transact business in Delaware, have derived substantial revenue from sales of pharmaceutical products in Delaware, and are expected to market their anti-PD-1 antibody product pembrolizumab in Delaware. On information and belief, Defendants have repeatedly availed themselves of the Delaware Courts.

12. Defendants reside in this judicial district and venue is proper in this district under 28 U.S.C. §§ 1391(b), (c), and/or 1400(b).

INVENTION OF METHODS FOR TREATING CANCER

13. On May 20, 2014, the United States Patent & Trademark Office ("USPTO") duly and legally issued United States Patent No. 8,728,474 (the "474 patent" (Exhibit 1)) titled "Immunopotentiative Composition." The inventors of the 474 patent showed for the first time that anti-PD-1 antibodies were useful in methods to treat cancer. Tasuku Honjo is a co-inventor and original co-assignee of the 474 patent. Ono is an original co-assignee and exclusive licensor of BMS under the 474 patent. BMS and Squibb are each exclusive licensees of one or more exclusionary rights under the 474 patent. The 474 patent claims methods for treating cancer with an antibody against PD-1.

14. Plaintiffs have put the invention of the 474 patent into practice by developing the breakthrough biologic drug nivolumab. Nivolumab is a monoclonal antibody that recognizes and binds to the PD-1 protein. When nivolumab binds to the PD-1 protein, that PD-1 protein cannot interact with its natural binding partners. Using nivolumab to block the interaction between PD-1 and its binding partners allows a more robust T cell response by the patient's own immune system.

15. Clinical testing of nivolumab confirms the remarkable promise of anti-PD-1 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).

16. Plaintiffs are continuing 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. The United States Food and Drug Administration ("FDA") granted Fast Track designation for nivolumab for treatment of melanoma, non-small cell lung cancer, and renal cell carcinoma (http://news.bms.com/press-release/rd-news/investigational-pd-1-immune-checkpoint-inhibitor-nivolumab-receives-us-fda-bre). The FDA has designated nivolumab as a Breakthrough Therapy for the treatment of certain patients with lymphoma (http://news.bms.com/press-release/rd-news/investigational-pd-1-immune-checkpoint-inhibitor-nivolumab-receives-us-fda-bre). BMS has announced that it expects to complete submission of its Biologics License Application (BLA) for nivolumab's use in treating non-small cell lung cancer by the end of 2014 (http://news.bms.com/press-release/rd-news/bristol-myers-squibb-announces-plans-third-quarter-submission-biologics-licens).

17. In Phase III clinical testing, patients with advanced melanoma who received nivolumab showed superior overall survival compared to those who did not, leading BMS to stop the clinical study early and make nivolumab available to all patients in the trial (http://news.bms.com/press-release/phase-3-first-line-melanoma-study-nivolumab-investigational-pd-1-checkpoint-inhibitor-). Based on these clinical results, BMS has announced plans to submit its BLA for nivolumab in the United States for certain melanoma patients in the

third quarter of 2014 (http://news.bms.com/press-release/rd-news/bristol-myers-squibb-announces-plans-third-quarter-submission-biologics-licens). Together, these clinical results confirm that the anti-PD-1 cancer treatments developed by the Plaintiffs can be used to save the lives of patients with a wide range of cancers.

MERCK'S INFRINGEMENT

18. Merck is planning to exploit the invention of the 474 patent with an anti-PD-1 antibody called pembrolizumab. On information and belief, Merck started developing pembrolizumab after Plaintiffs had made and started testing nivolumab, and Merck has since been engaged in efforts to meet the FDA regulatory requirements for marketing, distributing, offering for sale, and selling pembrolizumab for the treatment of cancer. According to Merck, pembrolizumab is a PD-1 antibody that works by blocking the PD-1 checkpoint to treat cancer.

19. On information and belief, Merck has known about the 474 patent and has known that the use of pembrolizumab will infringe claims of the 474 patent since at least approximately May 20, 2014, when the 474 patent was issued by the USPTO. In its August 7, 2014, 10-Q filing with the U.S. Securities and Exchange Commission ("SEC"), Merck & Co., Inc. acknowledged that the USPTO had granted the 474 patent (Merck & Co., Inc. U.S. Securities & Exchange Commission Form 10-Q at 22 (filed August 7, 2014)). In that same SEC filing, Merck & Co., Inc. admits that the use of pembrolizumab to treat cancer is covered by the European counterpart to the 474 patent (*id.* ("As previously disclosed, Ono Pharmaceutical Co. ("Ono") has a European patent (EP 1 537 878) ("'878") that broadly claims the use of an anti-PD-1 antibody, such as the Company's immunotherapy, pembrolizumab (MK-3475), for the treatment of cancer.")).

20. Merck and its affiliates have had knowledge of the family of patents that includes the 474 patent for many years and have instituted legal proceedings seeking to invalidate the corresponding patents in Europe. Merck initiated an opposition proceeding against European Patent EP 1 537 878 ("EP 878 patent"), a European counterpart of the 474 patent, in the European Patent Office on June 20, 2011. Merck made numerous submissions in that opposition proceeding and an oral hearing was held on June 4, 2014. On information and belief, Merck's outside counsel referred to the 474 patent during the oral hearing. That same day, the panel hearing oral argument rejected Merck's opposition and held the EP 878 patent valid.

21. On May 22, 2014, Merck's European affiliate filed a revocation action in the United Kingdom seeking to revoke the U.K. patent corresponding to the EP 878 patent. BMS has filed a counterclaim alleging infringement by pembrolizumab in that action.

22. On information and belief, Merck received approval from the FDA on September 4, 2014, to market pembrolizumab as a treatment for certain patients with melanoma. Merck's pembrolizumab is especially made for use in infringing the 474 patent and has no substantial non-infringing uses. By virtue of obtaining approval to market and sell pembrolizumab as a treatment for certain patients with melanoma, Merck has the specific intent to cause infringement of the 474 patent or, at a minimum, Merck has been willfully blind to the infringement of the 474 patent that will inevitably result.

23. On information and belief, Merck either has begun efforts to produce substantial supplies of pembrolizumab in anticipation of an imminent launch in the United States, and/or will soon begin, or has begun, manufacturing, distributing, using, offering for sale, selling, and/or importing in the United States the pembrolizumab antibody product to be prescribed and

used for the treatment of cancer. Upon information and belief, such pembrolizumab is being used and will be used for the treatment of cancer in the United States.

COUNT I: DECLARATORY JUDGMENT OF PATENT INFRINGEMENT

24. Plaintiffs incorporate by reference paragraphs 1-23 as if fully set forth herein.

25. As set forth above, a real, immediate, substantial, and justiciable controversy has arisen and now exists between the parties under the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202.

26. Merck is actively preparing to and will imminently infringe the 474 patent. As set forth above, on information and belief, by making meaningful preparations to market, make, use, sell, offer for sale, and/or import pembrolizumab in the United States for the treatment of cancer, Merck will imminently infringe the 474 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).

27. On information and belief, Merck has been aware of the 474 patent since at least approximately May 20, 2014, when the USPTO issued the 474 patent and Merck's imminent infringement is deliberate, willful, and in reckless disregard of valid patent claims of the 474 patent.

28. Plaintiffs will be injured by and will suffer substantial damages as a result of Merck's imminent infringement.

COUNT II: PATENT INFRINGEMENT

29. Plaintiffs incorporate by reference paragraphs 1-28 as if fully set forth herein.

30. A real, immediate, substantial, and justiciable controversy has arisen and now exists between the parties as to whether Merck is infringing the 474 patent.

31. On information and belief, Merck is marketing, making, using, selling, offering for sale, and/or importing pembrolizumab in the United States for the treatment of cancer. On information and belief, such pembrolizumab is being used for the treatment of cancer in the United States. As set forth above, Merck is thereby infringing the 474 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).

32. On information and belief, Merck has been aware of the 474 patent since at least approximately May 20, 2014, when the USPTO issued the 474 patent and Merck's infringement is deliberate, willful, and in reckless disregard of valid patent claims of the 474 patent.

33. Plaintiffs have been and will continue to be injured by and have been and will continue to suffer substantial damages as a result of Merck's infringement.

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 declaratory judgment that Defendants infringe and will infringe the 474 patent;

(b) entry of a judgment that Defendants infringe and will infringe the 474 patent;

(c) an award of damages sufficient to compensate Plaintiffs for infringement of the 474 patent, together with pre- and post-judgment interest and costs as fixed by the Court as provided by 35 U.S.C. § 284;

(d) entry of an order compelling Defendants to compensate Plaintiffs for any ongoing or future infringement of the 474 patent, in an amount and under terms appropriate for the circumstances;

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

(f) 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

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

Dated: November 21, 2014

Respectfully submitted,

FARNAN LLP

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