**UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| 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** |
| MERCK & CO., INC. and MERCK SHARP & DOHME CORP., | ) | |
| Defendants. | ) | |

**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 a declaratory judgment of 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. According to the United States Food & Drug Administration ("FDA"), "[l]ung cancer is the leading cause of cancer death in the United States, with an estimated 224,210 new diagnoses and 159,260 deaths in 2014. The most common type of lung cancer, [non-small cell lung cancer,] affects seven out of eight lung cancer patients" (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm436534.htm).

3. 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.

4. 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.

5. The invention at issue here covers using antibodies that bind to PD-1 ("anti-PD-1 antibodies") in a method for treating lung 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 lung cancer cells.

6. 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, and the first anti-PD-1 antibody approved in the United States for the treatment of lung cancer.

7. Merck is threatening to exploit that invention with a later-developed anti-PD-1 antibody. As described below, Merck is preparing to infringe Plaintiffs' patent for methods of treating lung cancer with anti-PD-1 antibodies.

**PARTIES**

8. 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.

9. 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 2000 Galloping Hill Rd., Kenilworth, New Jersey, 07053. 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 2000 Galloping Hill Rd., Kenilworth, New Jersey, 07053.

## JURISDICTION AND VENUE

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

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

12. 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, market their anti-PD-1 antibody product pembrolizumab in Delaware for the treatment of melanoma, and are expected to market pembrolizumab in Delaware for the treatment of lung cancer. On information and belief, Defendants have repeatedly availed themselves of the Delaware Courts.

13. 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

14. On June 30, 2015, the United States Patent & Trademark Office ("USPTO") duly and legally issued United States Patent No. 9,067,999 (the "999 patent" (Exhibit 1)) titled "Immunopotentiative Composition." The inventors of the 999 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 999 patent. Ono is an original co-assignee and exclusive licensor of BMS under the 999 patent. BMS and Squibb are each exclusive licensees of one or more

exclusionary rights under the 999 patent. The 999 patent claims methods for treating cancer with an antibody against PD-1.

15. Plaintiffs have put the invention of the 999 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.

16. 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). On December 22, 2104, the FDA approved nivolumab for treatment of advanced melanoma in the United States.

17. 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. These clinical results and the FDA's recent approval of nivolumab for the treatment of lung cancer confirm that the anti-PD-1 cancer treatments developed by the Plaintiffs can be used to save the lives of patients with lung cancer.

**MERCK'S FUTURE INFRINGEMENT**

18. Merck is planning to exploit the invention of the 999 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. Merck has received FDA approval to sell pembrolizumab in the United States for the treatment of melanoma, and 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 lung 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 999 patent and has known that the use of pembrolizumab will infringe claims of the 999 patent since June 30, 2015, when the 999 patent was issued by the USPTO and this declaratory judgment action was filed.

20. Merck and its affiliates have had knowledge of the family of patents that includes the 999 patent for many years and have instituted legal proceedings seeking to invalidate the corresponding patents in Europe. Merck initiated an opposition proceeding in the European Patent Office on June 20, 2011, against European Patent EP 1 537 878 ("EP 878 patent"), the European counterpart of U.S. Patent Number 8,728,474 (the "474 patent"), the 999 patent's parent patent. Merck made numerous submissions in that opposition proceeding and an oral

hearing was held on June 4, 2014. 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 September 4, 2014, the day Merck received approval to sell its pembrolizumab product in the Unites States for treatment of melanoma, Plaintiffs filed suit against Merck in this judicial district, asserting the 474 patent, which claims *inter alia* the use of a PD-1 antibody to treat melanoma.

23. On information and belief, on May 6, 2014, Merck filed a Biologics License Application ("BLA") seeking approval to use pembrolizumab to treat patients with advanced melanoma. The FDA granted priority review and set a target action date for review of Merck's BLA by October 28, 2014. On September 4, 2014, four months after Merck submitted its BLA, and nearly two months before the FDA's target action date, the FDA approved pembrolizumab as a treatment for certain patients with melanoma.

24. On information and belief, on April 19, 2015, Merck submitted a supplemental BLA seeking approval of pembrolizumab for the treatment of lung cancer.

25. On information and belief, on June 1, 2015, the FDA granted priority review of Merck's supplemental BLA seeking approval of pembrolizumab for the treatment of lung cancer and set a target action date of October 2, 2015.

26. According to Merck's press release announcing the FDA's priority review of Merck's supplemental BLA, the president of Merck Research Laboratories stated that "[w]e believe that data submitted to the FDA illustrate the significant potential of [pembrolizumab] to

treat advanced non-small cell lung cancer – and we look forward to working with the FDA to bring our anti-PD-1 therapy to patients afflicted with this devastating cancer" (http://www.mercknewsroom.com/news-release/oncology-newsroom/fda-accepts-supplemental-biologics-license-application-sbla-keytruda-).

27. By virtue of seeking imminent approval to market and sell pembrolizumab as a treatment for certain patients with lung cancer, Merck has the specific intent to cause infringement of the 999 patent or, at a minimum, Merck has been willfully blind to the infringement of the 999 patent that will inevitably result.

28. On information and belief, Merck 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 lung cancer. On information and belief, such pembrolizumab is currently being used in the United States for the treatment of melanoma, and will be used for the treatment of lung cancer in the United States immediately upon pembrolizumab's approval for the treatment of lung cancer.

**COUNT I: DECLARATORY JUDGMENT OF PATENT INFRINGEMENT**

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

30. 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.

31. Merck is actively preparing to and will imminently infringe the 999 patent. As set forth above, on information and belief, Merck has sought approval to sell pembrolizumab in the United States for the treatment of lung cancer, and Merck expects to receive that approval between today and October 2, 2015. 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 lung cancer, Merck will imminently infringe the 999 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 999 patent since June 30, 2015, when the USPTO issued the 999 patent. Should Merck choose to market, make, use, sell, offer for sale, and/or import pembrolizumab in the United States for the treatment of lung cancer following approval to do so, Merck's infringement will be deliberate, willful, and in reckless disregard of valid patent claims of the 999 patent.

33. Plaintiffs will be injured by and will suffer substantial damages as a result of Merck's imminent 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 999 patent;

(b) entry of an order compelling Defendants to compensate Plaintiffs for any ongoing or future infringement of the 999 patent, in an amount and under terms appropriate for the circumstances along with pre and post judgment interest and costs;

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

(d) 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

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

Dated: June 30, 2015

Respectfully submitted,

FARNAN LLP

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