UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BRISTOL-MYERS SQUIBB CO. and E. R. SQUIBB & SONS, L.L.C.,	)	
Plaintiffs,	)	C.A. No. _____
v.	)	**JURY TRIAL DEMANDED**
ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA UK LTD.,	)	
Defendants.	)	

COMPLAINT

Plaintiffs Bristol-Myers Squibb Co. ("BMS") and E. R. Squibb & Sons, L.L.C. ("Squibb") for their complaint for patent infringement against Defendants AstraZeneca Pharmaceuticals LP and AstraZeneca UK Ltd. (collectively, "Defendants" or "AstraZeneca"), hereby allege as follows:

INTRODUCTION

1. According to the United States Centers for Disease Control and Prevention, more than 1.6 million people in the United States are diagnosed with cancer each year (https://www.cdc.gov/chronicdisease/resources/publications/factsheets/cancer.htm). 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 infected or malignant cells through the activation or deactivation of various receptors on the T cell surface. One of the receptors that T cells express 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 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. When cancer cells are present, this pathway can prevent the immune system from eliminating those cancer cells. 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. Plaintiffs invented methods for treating cancer and methods for enhancing immune responses by administering antibodies that bind to PD-L1 ("anti-PD-L1 antibodies").

The inventions also cover using specific types of anti-PD-L1 antibodies 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. Plaintiffs also invented anti-PD-L1 antibodies with specific properties for use in methods of treatment and methods for enhancing immune responses.

6. 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.

7. Nivolumab is a monoclonal antibody that recognizes and binds to PD-1. When nivolumab binds to PD-1, it prevents PD-1 from binding to its ligands, e.g., PD-L1. Using nivolumab to block the interaction between PD-1 and its ligands enhances the T cell response generated by the patient's immune system.

8. 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 (OPDIVO) for the treatment of melanoma, a deadly form of skin cancer (https://www.cancerresearch.org/en-us/immunotherapy/timeline-of-progress). On December 22, 2014, the U.S. Food and Drug Administration ("FDA") approved nivolumab for treatment of advanced melanoma in the United States.

9. Plaintiffs have continued worldwide development of nivolumab for treatment of a broad range of cancers, including non-small cell lung cancer, urothelial carcinoma, renal cell carcinoma, head and neck cancer, malignant pleural mesothelioma, lymphoma, colorectal cancer, hepatocellular carcinomas, esophageal cancer, and gastric cancers. 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 (https://news.bms.com/news/details/2015/FDA-Approves-Opdivo-nivolumab-for-the-Treatment-of-Patients-with-Previously-Treated-Metastatic-Squamous-Non-Small-Cell-Lung-Cancer/default.aspx). 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. In Phase III clinical testing for urothelial carcinoma, median disease-free survival was nearly twice as long in patients who received nivolumab as compared to placebo (https://news.bms.com/news/details/2021/U.S.-Food-and-Drug-Administration-Approves-Opdivo-nivolumab-for-the-Adjuvant-Treatment-of-Patients-with-High-Risk-Urothelial-Carcinoma/default.aspx). On August 29, 2021, based at least in part on those clinical results, the FDA approved nivolumab to treat certain types of urothelial carcinoma. The clinical results and the FDA's 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.

10. AstraZeneca is exploiting Plaintiffs' inventions and infringing Plaintiffs' intellectual property rights by marketing a later-developed anti-PD-L1 antibody product,

IMFINZI (durvalumab), which is used in methods for treating cancer and for enhancing the immune response.

11. Since Plaintiffs and AstraZeneca are direct competitors in the field of immunotherapy, Plaintiffs have suffered, and continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca's infringement. Marking pursuant to 35 U.S.C. § 287 was not required because Plaintiffs' product OPDIVO is an anti-PD-1 antibody and is not a patented article under the asserted patents.

PARTIES

12. 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.

13. On information and belief, AstraZeneca Pharmaceuticals LP is a limited partnership organized under the laws of the State of Delaware, with its principal place of business at 1800 Concord Pike, Wilmington, Delaware 19803.

14. On information and belief, AstraZeneca UK Limited is a private limited company organized under the laws of England and Wales, with its registered office at 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge, United Kingdom, CB2 0AA.

15. AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited are in the business of manufacturing, marketing, distributing, offering for sale, and selling drug products that are distributed and sold throughout the United States, including in Delaware.

16. AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited are sophisticated pharmaceutical companies. On information and belief, AstraZeneca relies on and actively seeks patent protection for its products. On information and belief, AstraZeneca regularly enforces its patents and other intellectual property rights.

JURISDICTION AND VENUE

17. 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.

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

19. This Court has personal jurisdiction over AstraZeneca Pharmaceuticals LP because it is a Delaware entity located in Delaware.

20. This Court has jurisdiction over AstraZeneca UK Limited, *inter alia*, because its subsidiary and agent, AstraZeneca Pharmaceuticals LP, is incorporated in Delaware and, upon information and belief, markets and sells IMFINZI in Delaware as AstraZeneca UK Limited's authorized agent and under AstraZeneca UK Limited's direction and control.

21. On information and belief, AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited are engaged in a single business activity of biopharmaceuticals and are not separated into multiple operating segments. On information and belief, the biopharmaceuticals business of AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited consists of the discovery and development of products, which are then manufactured, marketed, and sold. On information and belief, all of these functional activities take place (and are managed) globally on a highly

integrated basis. On information and belief, these individual functional areas are not managed separately.

22. On information and belief, AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited have consented to jurisdiction in Delaware in one or more prior cases arising out of the manufacture, use, offer for sale, sale and/or importation of pharmaceutical products, including cases AstraZeneca initiated as the plaintiff.

23. Venue is proper in this district under 28 U.S.C. §§ 1391(c) and 1400(b).

THE PATENTS-IN-SUIT

24. On February 28, 2017, the USPTO duly and legally issued U.S. Patent No. 9,580,505 ("the '505 patent") titled "Human Monoclonal Antibodies to Programmed Death Ligand 1 (PD-L1)." A true and correct copy of the '505 patent is attached hereto as Exhibit 1. The '505 patent is assigned to E. R. Squibb & Sons, L.L.C.

25. The '505 patent issued from U.S. Application No. 14/807,522, filed on July 23, 2015, which is a divisional of U.S. Application No. 13/746,773, filed January 22, 2013 (now U.S. Patent No. 9,102,725), which is a divisional application of U.S. Application No. 13/091,936, filed April 21, 2011 (now U.S. Pat. No. 8,383,796), which is a divisional application of U.S. Application No. 11/917,727, filed June 9, 2008 (now U.S. Pat. No. 7,943,743), which is a national stage entry of PCT Application No. PCT/US2006/026046, filed June 30, 2006, which claims the benefit of U.S. Provisional Patent Application No. 60/696,426, filed July 1, 2005.

26. The claims of the '505 patent are generally directed to monoclonal antibodies that cross-compete with a specific reference antibody for binding to human PD-L1. By way of example, claim 1 of the '505 patent is:

An anti-PD-L1 monoclonal antibody, or an antigen-binding portion thereof, which cross-competes for binding to human PD-L1 with a reference antibody, wherein the reference antibody comprises:

(a) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:1 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:11;

(b) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:2 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:12;

(c) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:3 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:13;

(d) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:4 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:14;

(e) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:5 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:15;

(f) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:6 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:16;

(g) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:7 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:17;

(h) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:8 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:18;

(i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:9 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:19; or

(j) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:10 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:20; and

wherein the monoclonal antibody or antigen-binding portion thereof comprises a heavy chain variable region and a light chain variable region,

wherein a framework region of the heavy chain variable region is derived from a heavy chain variable germline sequence selected from a (a) human V_H 1-18 germline sequence; (b) human V_H 1-69 germline sequence; (c) human V_H 1-3 germline sequence; and (d) human V_H 3-9 germline sequence, or

a framework region of the light chain variable region is derived from a light chain variable germline sequence selected from a (a) human V_K L6 germline sequence, (b) human V_K L15 germline sequence, (c) human V_K A27 germline sequence, and (d) human V_K L18 germline sequence.

27. On February 28, 2017, the USPTO duly and legally issued U.S. Patent No. 9,580,507 ("the '507 patent") titled "Human Monoclonal Antibodies to Programmed Death Ligand 1 (PD-L1)." A true and correct copy of the '507 patent is attached hereto as Exhibit 2. The '507 patent is assigned to E. R. Squibb & Sons, L.L.C.

28. The '507 patent issued from U.S. Application No. 15/188,860, filed June 21, 2016, which is a divisional of U.S. Application No. 14/807,522, filed July 23, 2015 (now U.S. Patent No. 9,580,505), which is a divisional of U.S. Application No. 13/746,773, filed January 22, 2013 (now U.S. Pat. No. 9,102,725), which is a divisional application of U.S. Application No. 13/091,936, filed April 21, 2011 (now U.S. Pat. No. 8,383,796), which is a divisional application of U.S. Application No. 11/917,727, filed June 9, 2008 (now U.S. Pat. No. 7,943,743), which is a national stage entry of PCT Application No. PCT/US2006/026046, filed June 30, 2006, which claims the benefit of U.S. Provisional Patent Application No. 60/696,426, filed July 1, 2005.

29. The claims of the '507 patent are generally directed to monoclonal antibodies that cross-compete with a specific reference antibody for binding to human PD-L1. By way of example, claim 1 of the '507 patent is:

> A monoclonal anti-PD-L1 antibody, or an antigen-binding portion thereof, which cross-competes for binding to human PD-L1 with a reference antibody, wherein the reference antibody comprises:
> (a) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:1 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:11;
> (b) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:2 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:12;
> (c) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:3 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:13;

(d) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:4 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:14;
(e) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:5 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:15;
(f) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:6 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:16;
(g) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:7 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:17;
(h) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:8 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:18;
(i) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:9 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:19; or
(j) a heavy chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:10 and a light chain variable region comprising amino acids having the sequence set forth in SEQ ID NO:20; and

wherein the monoclonal anti-PD-L1 antibody or antigen-binding portion thereof comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises a framework region exhibiting at least 90% sequence identity to a framework region of the heavy chain variable region of the reference antibody and/or the VL comprises a framework region exhibiting at least 90% sequence identity to a framework region of the light chain variable region of the reference antibody.

30. On November 27, 2018, the USPTO duly and legally issued U.S. Patent No. 10,138,299 ("the '299 patent") titled "Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling." A true and correct copy of the '299 patent is attached hereto as Exhibit 3. The '299 patent is assigned to Bristol-Myers Squibb Company.

31. The '299 patent issued from U.S. Application No. 16/006,473, filed June 12, 2018, a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Pat. No. 9,212,224), which claims the benefit of U.S. Provisional Patent

Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

32. The claims of the ’299 patent are generally directed to methods of treating a tumor derived from bladder cancer by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the ’299 patent is:

> A method of treating a tumor in a human subject in need thereof, comprising administering to the subject about 10 mg/kg of an anti-PD-L1 antibody every 2 weeks, wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion;
> wherein the tumor is derived from a bladder cancer;
> and wherein the tumor is refractory to a platinum-based chemotherapy.

33. On June 4, 2019, the USPTO duly and legally issued U.S. Patent No. 10,308,714 (“the ’714 patent”) titled “Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling.” A true and correct copy of the ’714 patent is attached hereto as Exhibit 4. The ’714 patent is assigned to Bristol-Myers Squibb Company.

34. The ’714 patent issued from U.S. Application No. 16/024,340, filed June 29, 2018, which is a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Patent No. 9,212,224), which claims the benefit of U.S. Provisional Patent Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

35. The claims of the ’714 patent are generally directed to methods of treating a tumor derived from a bladder cancer by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the ’714 patent is:

> A method of treating a tumor in a human subject, comprising administering to the subject a therapeutically effective amount of an anti-PD-L1 antibody; wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion;

> wherein the tumor is derived from a bladder cancer; and wherein the tumor is refractory to a platinum based chemotherapy.

36. On April 23, 2019, the USPTO duly and legally issued U.S. Patent No. 10,266,594 ("the '594 patent") titled "Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling." A true and correct copy of the '594 patent is attached hereto as Exhibit 5. The '594 patent is assigned to Bristol-Myers Squibb Company.

37. The '594 patent issued from U.S. Application No. 16/213,954, filed December 7, 2018, which is a continuation of U.S. Application No. 16/006,365, filed June 12, 2018 (now U.S. Patent No. 10,316,090), which is a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Patent No. 9,212,224), which claims the benefit of U.S. Provisional Patent Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

38. The claims of the '594 patent are generally directed to methods of treating a tumor derived from a cancer of the renal pelvis by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the '594 patent is:

> A method of treating a tumor in a human subject in need thereof, comprising administering to the subject a therapeutically effective amount of an anti-PD-L1 antibody; wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion; wherein the tumor is derived from a cancer of the renal pelvis; and wherein the tumor is refractory to a platinum based chemotherapy.

39. On April 23, 2019, the USPTO duly and legally issued U.S. Patent No. 10,266,595 ("the '595 patent") titled "Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling." A true and correct copy of the '595 patent is attached hereto as Exhibit 6. The '595 patent is assigned to Bristol-Myers Squibb Company.

40. The ’595 patent issued from U.S. Application No. 16/213,960, filed December 7, 2018, which is a continuation of U.S. Application No. 16/006,365, filed June 12, 2018 (now U.S. Patent No. 10,316,090), which is a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Patent No. 9,212,224), which claims the benefit of U.S. Provisional Patent Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

41. The claims of the ’595 patent are generally directed to methods of treating a tumor derived from a cancer of the ureter by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the ’595 patent is:

> A method of treating a tumor in a human subject in need thereof, comprising administering to the subject a therapeutically effective amount of an anti-PD-L1 antibody; wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion; wherein the tumor is derived from a cancer of the ureter; and wherein the tumor is refractory to a platinum based chemotherapy.

42. On April 23, 2019, the USPTO duly and legally issued U.S. Patent No. 10,266,596 (“the ’596 patent”) titled “Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling.” A true and correct copy of the ’596 patent is attached hereto as Exhibit 7. The ’596 patent is assigned to Bristol-Myers Squibb Company.

43. The ’596 patent issued from U.S. Application No. 16/213,965, filed December 7, 2018, which is a continuation of U.S. Application No. 16/006,365, filed June 12, 2018 (now U.S. Patent No. 10,316,090), which is a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Patent No. 9,212,224), which claims the benefit of U.S. Provisional Patent Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

44. The claims of the ’596 patent are generally directed to methods of treating a tumor derived from a cancer of the urethra by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the ’596 patent is:

> A method of treating a tumor in a human subject in need thereof, comprising administering to the subject a therapeutically effective amount of an anti-PD-L1 antibody; wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion; wherein the tumor is derived from a cancer of the urethra; and wherein the tumor is refractory to a platinum based chemotherapy.

45. On June 18, 2019, the USPTO duly and legally issued U.S. Patent No. 10,323,092 (“the ’092 patent”) titled “Cancer Immunotherapy by Disrupting PD-1/PD-L1 Signaling.” A true and correct copy of the ’092 patent is attached hereto as Exhibit 8. The ’092 patent is assigned to Bristol-Myers Squibb Company.

46. The ’092 patent issued from U.S. Application No. 16/006,493, filed June 12, 2018, which is a continuation of U.S. Application No. 14/950,748, filed November 24, 2015 (now U.S. Patent No. 10,072,082), which is a divisional of U.S. Application No. 13/892,671, filed May 13, 2013 (now U.S. Patent No. 9,212,224), which claims the benefit of U.S. Provisional Patent Application No. 61/790,747, filed on March 15, 2013, and U.S. Provisional Patent Application No. 61/647,442, filed May 15, 2012.

47. The claims of the ’092 patent are generally directed to methods of treating a late stage non-small cell lung cancer tumor by administering an anti-PD-L1 antibody to the subject. By way of example, claim 1 of the ’092 patent is:

> A method of treating a late stage non-small cell lung cancer (NSCLC) tumor in a human subject, comprising administering to the subject about 10 mg/kg of an anti-PD-L1 antibody every 2 weeks, wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion; wherein the subject is pretreated for a chemotherapy and a radiotherapy; and wherein at least 1% of tumor cells in the tumor exhibit membrane PD-L1 expression.

ASTRAZENECA'S IMFINZI PRODUCT

48. AstraZeneca UK Limited is the holder of Biologics License Application ("BLA") No. 761069 for IMFINZI (durvalumab). According to its prescribing information, IMFINZI contains a PD-L1 blocking antibody named durvalumab that is indicated for treating patients with specific types of cancer. The FDA-approved label for IMFINZI indicates that IMFINZI is manufactured for AstraZeneca Pharmaceuticals LP by AstraZeneca UK Limited. On information and belief, AstraZeneca Pharmaceuticals LP is marketing, using, distributing, offering for sale, selling, and importing IMFINZI in the United States as AstraZeneca UK Limited's authorized agent.

49. On May 1, 2017, the FDA approved IMFINZI as a treatment for patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.[1] The prescribing information that AstraZeneca provided and that the FDA approved in May 2017 instructed that IMFINZI was to be administered in a 10 mg/kg dose as an intravenous infusion over 60 minutes every 2 weeks to treat urothelial carcinoma.[2]

50. On information and belief AstraZeneca began marketing IMFINZI for the treatment of urothelial carcinoma according to the prescribing information in the United States on May 1, 2017.

51. On February 16, 2018, the FDA approved IMFINZI as a treatment for patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not

[1] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/761069Orig1s000ltr.pdf.
[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761069s000lbl.pdf.

progressed following concurrent platinum-based chemotherapy and radiation therapy.[3] The prescribing information that AstraZeneca provided and the FDA approved for the use of IMFINZI to treat non-small cell lung cancer indicates that IMFINZI is to be administered in a 10 mg/kg dose as an intravenous infusion over 60 minutes every 2 weeks.[4]

52. On information and belief AstraZeneca began marketing IMFINZI for the treatment of unresectable Stage III non-small cell lung cancer in the United States on February 16, 2018, and continues to market IMFINZI for the treatment of unresectable Stage III non-small cell lung cancer today.

53. On November 18, 2020, the FDA approved a change to IMFINZI's prescribing information providing for the addition of an alternate treatment schedule of 1500 mg every 4 weeks for stage 3 unresectable non-small cell lung cancer and urothelial carcinoma.[5] That alternative, optional treatment schedule can only be used with patients having a body weight of 30 kg or more.[6] On information and belief, doctors have continued to prescribe IMFINZI at a dose of 10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks as described in the prescribing information.

54. On February 19, 2021, the FDA approved prescribing information for IMFINZI that removed the indication for patients having locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with

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[3] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/761069Orig1s002ltr.pdf.

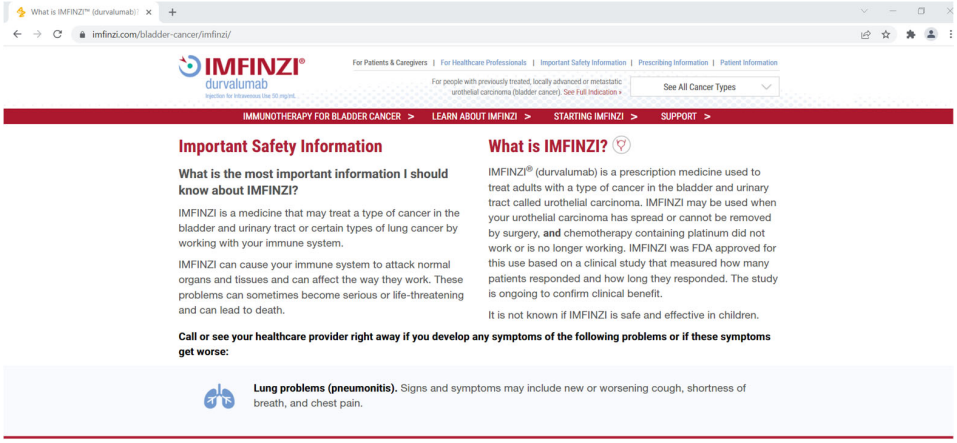
[4] https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761069s002lbl.pdf; https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761069s028lbl.pdf.

[5] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/761069Orig1s023,%20s024,%20s025ltr.pdf.

[6] https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761069s023s024s025lbl.pdf.

platinum-containing chemotherapy.[7] But AstraZeneca continues to specifically teach and market the use of IMFINZI to treat urothelial carcinoma. AstraZeneca hosts a website that explains that IMFINZI can be used to treat urothelial carcinoma.[8]

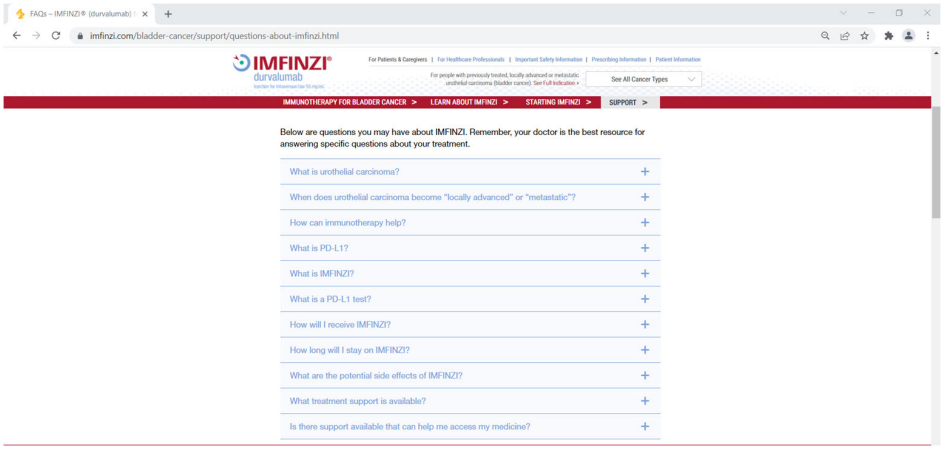
55. The AstraZeneca website https://www.imfinzi.com/bladder-cancer/imfinzi/, depicted below, a copy of which is attached hereto as Exhibit 9, was accessible at least as of the filing of this complaint on March 17, 2022. That website states that "IMFINZI is a medicine that may treat a type of cancer in the bladder and urinary tract or certain types of lung cancer by working with your immune system."



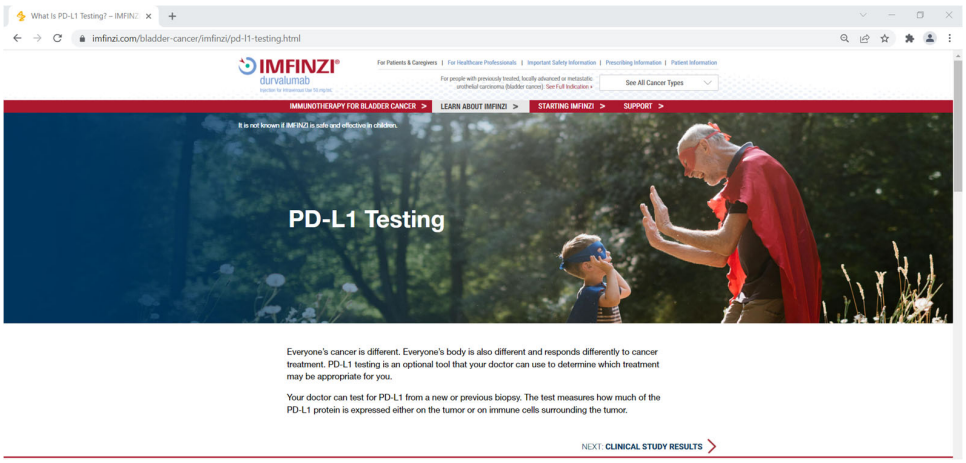
56. Another AstraZeneca website, https://www.imfinzi.com/bladder-cancer/support/questions-about-imfinzi.html, depicted below, a copy of which is attached hereto as Exhibit 10, was accessible at least as of the filing of this complaint on March 17, 2022. That website provides answers to frequently asked questions about IMFINZI and urothelial carcinoma.

[7] https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761069s029lbl.pdf.

[8] https://www.imfinzi.com/bladder-cancer/imfinzi/ (last visited March 17, 2022).



57. Another AstraZeneca website, https://www.imfinzi.com/bladder-cancer/imfinzi/pd-l1-testing.html, depicted below, a copy of which is attached hereto as Exhibit 11, was accessible at least as of the filing of this complaint on March 17, 2022. That website explains that doctors can test for PD-L1 expression on tumor cells.



58. On information and belief, doctors continued to prescribe IMFINZI for urothelial carcinoma after February 19, 2021, and they continue to do so today.

59. The active ingredient in AstraZeneca's IMFINZI product is the anti-PD-L1 antibody durvalumab. Durvalumab is a human IgG1κ monoclonal antibody that binds to human PD-L1, thereby inhibiting the interaction of PD-L1 with PD-1. Durvalumab interferes with the

PD-L1/PD-1 mediated inhibition of the immune response in order to produce an anti-tumor immune response.

60. Durvalumab cross competes with the anti-PD-L1 antibody 12A4 (also known as BMS-936559) for binding to human PD-L1.

IMFINZI Infringes the '505 Patent

61. As described above, on information and belief, AstraZeneca is currently manufacturing, distributing, using, offering for sale, selling, and/or importing in the United States the IMFINZI antibody product to be prescribed and used for the treatment of cancer according to the IMFINZI prescribing information.

62. As described above, durvalumab is a human, anti-PD-L1 monoclonal antibody with a heavy chain variable region and a light chain variable region that cross-competes for binding to human PD-L1 with a reference antibody or antigen-binding portion thereof which comprises a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO:2 and a light chain variable region having the amino acid sequence set forth in SEQ ID NO:12, identified in the '505 patent as 12A4. Public information about the amino acid sequence of durvalumab shows that it includes framework regions in both its heavy and light chains that have significant and/or complete identity with the germline sequences identified in claim 1. Durvalumab therefore has a framework region derived from one or more of the germline sequences recited in claim 1. Durvalumab also has heavy and light chains with a framework region selected from the group of sequences identified in claim 29 of the '505 patent. Therefore, IMFINZI infringes at least claims 1, 28-29, and 41 of the '505 patent.

63. Based on public information, durvalumab includes one or more framework regions of the heavy chain variable region exhibiting greater than 90% sequence identity to at

least one of the germline sequences recited in claim 2, and less than 10 amino acid differences from the corresponding germline sequence. Therefore, IMFINZI infringes at least claims 2 and 4 of the ’505 patent.

64. Based on public information, durvalumab includes one or more framework regions of the light chain variable region exhibiting greater than 90% sequence identity, and greater than 95% sequence identity to at least one of the germline sequences recited in claims 5 and 6, and less than 10 amino acid differences from the corresponding germline sequence. Therefore, IMFINZI infringes at least claims 5-7 of the ’505 patent.

65. Based on public information, durvalumab has framework regions of the light chain variable region selected from the group of sequences set forth for each of claims 30, 31, and 32. Therefore, IMFINZI infringes at least claims 30-32 of the ’505 patent.

66. Based on public information, durvalumab has framework regions of the heavy chain variable region selected from the group of sequences set forth for each of claims 34 and 36. Therefore, IMFINZI infringes at least claims 34 and 36 of the ’505 patent.

67. Based on public information, durvalumab binds to human PD-L1 with a K_D of less than 1 nM, corresponding to 1×10^{-9} M. That K_D is less than 5×10^{-9} M, less than 2×10^{-9} M, and less than 1×10^{-9} M. Therefore, IMFINZI infringes at least claims 21-23 and 37-39 of the ’505 patent. As set forth in the ’505 patent, the reference antibody which comprises a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO:2 and a light chain variable region having the amino acid sequence set forth in SEQ ID NO:12 (identified in the ’505 patent as 12A4) has a K_D less than 5×10^{-9} M, and less than 2×10^{-9} M. Therefore, IMFINZI infringes at least claims 24-25 of the ’505 patent.

68. On information and belief, AstraZeneca has known about the ’505 patent since as early as February 28, 2017, when the ’505 patent issued, but in any event, at least before receiving a copy of this complaint.

69. AstraZeneca has had knowledge of the ’505 patent since the ’505 patent issued because U.S. Publication No. 2009/0055944, the publication of U.S. Patent Application No. 11/917,727 (“the ’727 Application”) was included in a March 27, 2013 information disclosure statement filed during the pendency of the application that led to AstraZeneca’s U.S. Patent No. 8,779,108 (the “’108 patent”). The ’505 patent claims priority to, is a direct descendant of, and contains claims similar to the ’727 Application. The ’108 patent describes the development of durvalumab, specifically claims durvalumab, and is assigned to MedImmune, Limited, a company that, on information and belief, is a subsidiary of AstraZeneca and developed durvalumab. In addition, AstraZeneca was mailed an International Search Report from the WIPO on February 11, 2011 in connection with its International Patent Application No. PCT/US2010/058007 (“the ’007 PCT”) that identified the ’727 Application as a reference of particular relevance in view of which certain of AstraZeneca’s claims could not be considered novel or could not be considered to involve an inventive step when taken with one or more other documents. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

70. Moreover, AstraZeneca has had knowledge of the ’505 patent since the ’505 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and

non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

71. AstraZeneca has had knowledge of the '505 patent since the '505 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, AstraZeneca monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '505 patent at that point. Therefore, AstraZeneca would have had knowledge of the '505 patent since at least that time. AstraZeneca also has had knowledge of the '505 patent since the '505 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

72. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the ’505 patent since the ’505 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI, including the ’108 patent. The ’727 Application, from which the ’505 patent is a direct descendant, was cited during prosecution of the ’108 patent. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the ’505 patent existed.

73. The ’727 Application, from which the ’505 patent is a direct descendant, was cited during prosecution of the ’108 patent, which covers AstraZeneca’s IMFINZI product. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’505 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’505 patent. If AstraZeneca did not have actual knowledge of the existence of the ’505 patent, it is because AstraZeneca was willfully blind to the existence of the ’505 patent.

74. AstraZeneca has known that IMFINZI, and the use of IMFINZI in patients to treat cancer infringes at least claims 1-2, 4-7, 21-25, 28-32, 34, 36-39, and 41 of the ’505 patent since as early as February 28, 2017, when the ’505 patent issued, but in any event, before receiving a

copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, AstraZeneca was aware of the amino acid sequence of IMFINZI. On information and belief, AstraZeneca was aware of public information since at least 2018 that durvalumab cross competes with 12A4. Accordingly, once AstraZeneca knew of the ’505 patent, AstraZeneca knew that IMFINZI infringed the ’505 patent.

75. If AstraZeneca did not have actual knowledge that IMFINZI, and the use of IMFINZI in patients to treat cancer, infringes at least claims 1-2, 4-7, 21-25, 28-32, 34, 36-39, and 41 of the ’505 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’505 patent or was willfully blind to the existence of the ’505 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers an anti-PD-L1 antibody with sequences found in IMFINZI, AstraZeneca subjectively believed that there was a high probability that IMFINZI and the use of IMFINZI would infringe the ’505 patent. Based on the similarity between the ’505 patent’s claims and IMFINZI’s amino acid sequence, and public information since at least 2018 that durvalumab cross competes with 12A4, the only way that AstraZeneca would not know that the use of IMFINZI infringed the ’505 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’505 patent.

76. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-2, 4-7, 21-25, 28-32, 34, 36-39, and 41 of the ’505 patent. IMFINZI is especially made, and has been made, to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’505 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a

product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’505 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’505 patent.

77. Through its prescribing information and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’505 patent. AstraZeneca has had and continues to have the specific intent to infringe, willfully infringe, and actively induce others to infringe the ’505 patent.

IMFINZI Infringes the ’507 Patent

78. As described above, on information and belief, AstraZeneca is currently manufacturing, distributing, using, offering for sale, selling, and/or importing in the United States the IMFINZI antibody product to be prescribed and used for the treatment of cancer according to the IMFINZI prescribing information.

79. As described above, durvalumab is a human, monoclonal anti-PD-L1 antibody with a VH of IgG1 isotype that cross-competes for binding to human PD-L1 with at least the reference antibody or antigen-binding portion thereof which comprises a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO:2 and a light chain variable region having the amino acid sequence set forth in SEQ ID NO:12. Based on public information, the sequence of durvalumab includes sequences recited in each of claims 1-7, 9, 11, 12, and 22. Therefore, IMFINZI infringes at least claims 1-7, 9, 11, 12, and 22 of the ’507 patent.

80. Based on public information, durvalumab binds to human PD-L1 with a K_D of less than 1 nM, corresponding to 1×10^{-9} M. That K_D is less than 5×10^{-9} M, less than 2×10^{-9} M, and less than 1×10^{-9} M. Therefore, IMFINZI infringes at least claims 15-17 of the ’507

patent. As set forth in the ’507 patent, the reference antibody which comprises a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO:2 and a light chain variable region having the amino acid sequence set forth in SEQ ID NO:12 (identified in the ’507 patent as 12A4) has a K_D less than 5×10^{-9} M, and less than 2×10^{-9} M. Therefore, IMFINZI infringes at least claims 18-19 of the ’507 patent.

81. As described above, the prescribing information for IMFINZI discloses that IMFINZI is administered in a 10 mg/kg dose as an intravenous infusion over 60 minutes every 2 weeks. According to its prescribing information, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. IMFINZI therefore infringes at least claims 27 and 28 of the ’507 patent.

82. On information and belief, AstraZeneca has known about the ’507 patent since as early as February 28, 2017, when the ’507 patent issued, but in any event, at least before receiving a copy of this complaint.

83. AstraZeneca has had knowledge of the ’507 patent since the ’507 patent issued because U.S. Publication No. 2009/0055944, the publication of U.S. Patent Application No. 11/917,727 (“the ’727 Application”) was included in a March 27, 2013 information disclosure statement filed during the pendency of the application that led to AstraZeneca’s U.S. Patent No. 8,779,108 (the “’108 patent”). The ’507 patent claims priority to, is a direct descendant of, and contains claims similar to the ’727 Application. The ’108 patent describes the development of

durvalumab, specifically claims durvalumab, and is assigned to MedImmune, Limited, a company that, on information and belief is a subsidiary of AstraZeneca and developed durvalumab. In addition, AstraZeneca was mailed an International Search Report from the WIPO on February 11, 2011 in connection with its International Patent Application No. PCT/US2010/058007 ("the '007 PCT") that identified the '727 Application as a reference of particular relevance in view of which certain of AstraZeneca's claims could not be considered novel or could not be considered to involve an inventive step when taken with one or more other documents. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI.

84. Moreover, AstraZeneca has had knowledge of the '507 patent since the '507 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

85. AstraZeneca has had knowledge of the '507 patent since the '507 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, AstraZeneca monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more

patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '507 patent at that point. Therefore, AstraZeneca would have had knowledge of the '507 patent since at least that time. AstraZeneca also has had knowledge of the '507 patent since the '507 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

86. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '507 patent since the '507 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI, including the '108 patent. The '727 Application, from which the '507 patent is a direct descendant, was cited during prosecution of the '108 patent. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies

to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the ’507 patent existed.

87. The ’727 Application, from which the ’507 patent is a direct descendant, was cited during prosecution of the ’108 patent, which covers AstraZeneca’s IMFINZI product. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’507 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’507 patent. If AstraZeneca did not have actual knowledge of the existence of the ’507 patent, it is because AstraZeneca was willfully blind to the existence of the ’507 patent.

88. AstraZeneca has known that IMFINZI, and the use of IMFINZI in patients to treat cancer infringes at least claims 1-7, 9, 11, 12, 15-19, 22, and 27-28 of the ’507 patent since as early as February 28, 2017, when the ’507 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, AstraZeneca was aware of the amino acid sequence of IMFINZI. On information and belief, AstraZeneca was aware of public information since at least 2018 that durvalumab cross competes with 12A4. Accordingly, once AstraZeneca knew of the ’507 patent, AstraZeneca knew that IMFINZI infringed the ’507 patent.

89. If AstraZeneca did not have actual knowledge that IMFINZI, and the use of IMFINZI in patients to treat cancer, infringes at least claims 1-7, 9, 11, 12, 15-19, 22, and 27-28

of the ’507 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’507 patent or was willfully blind to the existence of the ’507 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers an anti-PD-L1 antibody with sequences found in IMFINZI, AstraZeneca subjectively believed that there was a high probability that IMFINZI and the use of IMFINZI would infringe the ’507 patent. Based on the similarity between the ’507 patent’s claims and IMFINZI’s amino acid sequence, and public information since at least 2018 that durvalumab cross competes with 12A4, the only way that AstraZeneca would not know that the use of IMFINZI infringed the ’507 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’507 patent.

90. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-7, 9, 11, 12, 15-19, 22, and 27-28 of the ’507 patent. IMFINZI is especially made, and has been made, to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is, and has been, especially made for use to infringe the claims of the ’507 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’507 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’507 patent.

91. Through its prescribing information and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’507 patent. AstraZeneca has had and continues to have the specific intent to infringe, willfully infringe, and actively induce others to infringe the ’507 patent.

The Use of IMFINZI Infringes the '299 Patent

92. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be prescribed and used for the treatment of urothelial carcinoma, including tumors derived from a bladder cancer, according to IMFINZI's prescribing information from 2017 to 2021 and according to AstraZeneca's instructions via its websites, even after the prescribing information was adjusted in 2021, as described above.

93. As described above, and according to prescribing information for IMFINZI, IMFINZI is an anti-PD-L1 antibody used for treating a tumor in a subject in need of treatment. IMFINZI was specifically indicated for the treatment of urothelial carcinoma, a type of cancer in the bladder and urinary tract. IMFINZI is specifically indicated for patients who have disease progression during or following platinum-containing chemotherapy. The medication guide included with IMFINZI's prescribing information from 2017 to 2021 and instructions provided by AstraZeneca as described above informs patients that IMFINZI may be used when the patient has tried chemotherapy that contains platinum and it did not work or is no longer working.

94. As described above, and according to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks for the treatment of urothelial carcinoma.

95. On information and belief, IMFINZI has been used according to the instructions in its prescribing information from 2017 to 2021 and current instructions. The use of IMFINZI according to the instructions in its prescribing information from 2017 to 2021 and current instructions infringes at least claim 1 of the '299 patent.

96. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered for locally advanced or metastatic urothelial carcinoma. The use of IMFINZI according to its prescribing information and current instructions therefore infringes at least claims 2-4 of the ’299 patent.

97. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered for use until disease progression or unacceptable toxicity. The prescribing information included data from a urothelial carcinoma clinical study. That data informed physicians that all patients received IMFINZI for up to 12 months or until unacceptable toxicity or disease progression. In that clinical study, tumor assessments were performed at weeks 6, 12, 16, and then every 8 weeks for the first year and every 12 weeks thereafter. On information and belief, patients outside of clinical studies have been treated according to the IMFINZI’s prescribing information for more than 12 weeks. The use of IMFINZI according to the prescribing information therefore infringes at least claim 5 of the ’299 patent.

98. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to the prescribing information therefore infringes at least claims 6-9 of the ’299 patent.

99. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, PD-L1 can be expressed on both tumor cells and tumor-associated cells in the tumor microenvironment. In the urothelial carcinoma clinical study reported in the prescribing information, more than half of the patients were classified as "PD-L1 high." If immune cells involved greater than 1% of the tumor area, the patient was classified as "PD-L1 high" when greater than or equal to 25% of the tumor cells or immune cells expressed PD-L1. If immune cells involved less than or equal to 1% of the tumor area, the patient was classified as "PD-L1 high" when greater than or equal to 25% of the tumor cells or 100% of immune cells expressed PD-L1. IMFINZI's prescribing information thus instructs doctors to use IMFINZI to treat a patient when at least 1% (claim 10) or 5% (claim 11) of the tumor cells exhibit membrane PD-L1 expression. Accordingly, use of IMFINZI to treat patients where at least 1% or at least 5% of the tumor cells exhibit membrane PD-L1 expression according to the prescribing information infringes at least claims 10 and 11 of the '299 patent.

100. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered to adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy. The clinical study reported in the prescribing information from 2017 to 2021 explained that 70% of patients had received prior cisplatin therapy, 30% had received prior carboplatin therapy, and 35% had received greater than or equal to 2 prior lines of systemic therapy. IMFINZI's prescribing information from 2017 to 2021 and current instructions thus instruct doctors to use IMFINZI to treat a patient where the patient's tumor is refractory to cisplatin, carboplatin, both cisplatin and carboplatin, or platinum-based doublet chemotherapy.

The use of IMFINZI to treat such patients according to IMFINZI's prescribing information from 2017 to 2021 and current instructions, infringes at least claims 22 and 23 of the '299 patent.

101. On information and belief, AstraZeneca has known about the '299 patent since as early as November 27, 2018, when the '299 patent issued, but in any event, at least before receiving a copy of this complaint.

102. AstraZeneca has had knowledge of the '299 patent since the '299 patent issued because International Publication No. WO2013/173223 (International Application No. PCT/US2013/040764), which claims priority to the same provisional applications as the '299 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca's own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the '299 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody and claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 ("the '040 patent"), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the '040 patent at the United States Patent & Trademark Office is "AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606." On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune's GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and

the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI.

103. Moreover, AstraZeneca has had knowledge of the '299 patent since the '299 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

104. AstraZeneca has had knowledge of the '299 patent since the '299 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '299 patent's family at that point. Therefore, AstraZeneca would have had knowledge of the '299 patent since at least that time. AstraZeneca also has had knowledge of the '299 patent since the '299 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing

agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

105. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '299 patent since the '299 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the '299 patent existed.

106. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI.

"AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the '299 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the '299 patent. If AstraZeneca did not have actual knowledge of the existence of the '299 patent, it is because AstraZeneca was willfully blind to the existence of the '299 patent.

107. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1-11 and 22-23 of the '299 patent since as early as November 27, 2018, when the '299 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the '299 patent are found directly in IMFINZI's prescribing information. Accordingly, once AstraZeneca knew of the '299 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the '299 patent.

108. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1-11 and 22-23 of the '299 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the '299 patent or was willfully blind to the existence of the '299 patent. AstraZeneca is a sophisticated company and upon

learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI's prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the '299 patent. Based on the similarity between the '299 patent's claims and IMFINZI's prescribing information, the only way that AstraZeneca would not know that the use of IMFINZI infringed the '299 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the '299 patent.

109. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-11 and 22-23 of the '299 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the '299 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the '299 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the '299 patent.

110. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the '299 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the '299 patent.

The Use of IMFINZI Infringes the '714 Patent

111. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be

prescribed and used for the treatment of urothelial carcinoma, including tumors derived from a bladder cancer, according to IMFINZI's prescribing information from 2017 to 2021 and according to AstraZeneca's instructions on its website even after the prescribing information was adjusted in 2021, as described above.

112. As described above, and according to prescribing information for IMFINZI, IMFINZI is an anti-PD-L1 antibody used for treating a tumor in a subject in need of treatment. IMFINZI was specifically indicated for the treatment of urothelial carcinoma, a type of cancer in the bladder and urinary tract. IMFINZI is specifically indicated for patients who have disease progression during or following platinum-containing chemotherapy. The medication guide included with IMFINZI's prescribing information from 2017 to 2021 and current instructions informs patients that IMFINZI may be used when the patient has tried chemotherapy that contains platinum and it did not work or is no longer working.

113. As described above, and according to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks for the treatment of urothelial carcinoma. The clinical study described in IMFINZI's prescribing information explained that 17% of patients responded to treatment.

114. On information and belief, IMFINZI has been used according to the instructions in its prescribing information from 2017 to 2021 and current instructions. The use of IMFINZI according to the instructions in its prescribing information from 2017 to 2021 and current instructions infringes at least claim 1 of the '714 patent.

115. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered for locally advanced or metastatic urothelial

carcinoma. The use of IMFINZI according to its prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 2-4 of the ’714 patent.

116. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to its prescribing information from 2017 to 2021 current instructions therefore infringes at least claims 6-9 of the ’714 patent.

117. According to IMFINZI’s prescribing information from 2017 to 2021 and current instructions, PD-L1 can be expressed on both tumor cells and tumor-associated cells in the tumor microenvironment. In the urothelial carcinoma clinical study reported in the prescribing information, more than half of the patients were classified as “PD-L1 high.” If immune cells involved greater than 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or immune cells expressed PD-L1. If immune cells involved less than or equal to 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or 100% of immune cells expressed PD-L1. IMFINZI’s prescribing information thus instructs doctors to use IMFINZI to treat a patient when at least 1% (claim 10) or 5% (claim 11) of the tumor cells exhibit membrane PD-L1 expression. Accordingly, use of IMFINZI to treat patients where at least 1% or at least 5% of the tumor cells exhibit membrane PD-L1 expression according to the prescribing information infringes at least claims 10 and 11 of the ’714 patent.

118. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered to adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy. The clinical study reported in the prescribing information explained that 70% of patients had received prior cisplatin therapy, 30% had received prior carboplatin therapy, and 35% had received greater than or equal to 2 prior lines of systemic therapy. Based on the clinical study presented in the prescribing information, IMFINZI's prescribing information instructs doctors to use IMFINZI to treat a patient where the platinum-based chemotherapy is cisplatin, carboplatin, or both cisplatin and carboplatin. IMFINZI's prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient where the patient's tumor is refractory to cisplatin, carboplatin, or both cisplatin and carboplatin. The use of IMFINZI to treat such patients according to IMFINZI's prescribing information from 2017 to 2021 and current instructions, infringes at least claim 23 of the '714 patent.

119. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, if patients experience certain adverse reactions from taking IMFINZI, their dose can be modified. Specifically, the prescribing information instructs the doctor to administer various corticosteroid treatments depending on the adverse reaction. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claim 24 of the '714 patent.

120. On information and belief, AstraZeneca has known about the '714 patent since as early as June 4, 2019, when the '714 patent issued, but in any event, at least before receiving a copy of this complaint.

121. AstraZeneca has had knowledge of the ’714 patent since the ’714 patent issued because International Publication No. WO2013/173223 (International Application No. PCT/US2013/040764), which claims priority to the same provisional applications as the ’714 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca’s own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the ’714 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody and claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 (“the ’040 patent”), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the ’040 patent at the United States Patent & Trademark Office is “AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606.” On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune’s GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

122. Moreover, AstraZeneca has had knowledge of the ’714 patent since the ’714 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-

L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

123. AstraZeneca has had knowledge of the '714 patent since the '714 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '714 patent's family at that point, and the '714 patent when it issued shortly thereafter. Therefore, AstraZeneca would have had knowledge of the '714 patent since at least that time. AstraZeneca also has had knowledge of the '714 patent since the '714 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By

December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

124. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '714 patent since the '714 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the '714 patent existed.

125. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the

use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’714 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’714 patent. If AstraZeneca did not have actual knowledge of the existence of the ’714 patent, it is because AstraZeneca was willfully blind to the existence of the ’714 patent.

126. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, and 23-24 of the ’714 patent since as early as June 4, 2019, when the ’714 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the ’714 patent are found directly in IMFINZI’s prescribing information. Accordingly, once AstraZeneca knew of the ’714 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the ’714 patent.

127. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, and 23-24 of the ’714 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’714 patent or was willfully blind to the existence of the ’714 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI’s prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the ’714 patent. Based on the similarity between the ’714 patent’s claims and IMFINZI’s prescribing information, the only

way that AstraZeneca would not know that the use of IMFINZI infringed the ’714 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’714 patent.

128. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-4, 6-11, and 23-24 of the ’714 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’714 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’714 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’714 patent.

129. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’714 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the ’714 patent.

The Use of IMFINZI Infringes the ’594 Patent

130. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be prescribed and used for the treatment of urothelial carcinoma, including tumors derived from a cancer of the renal pelvis, according to IMFINZI’s prescribing information from 2017 to 2021 and according to AstraZeneca’s instructions on its website even after the prescribing information was adjusted in 2021, as described above.

131. As described above, and according to prescribing information for IMFINZI from 2017 to 2021 and current instructions, IMFINZI is an anti-PD-L1 antibody used for treating a tumor in a subject in need of treatment. IMFINZI was specifically indicated for the treatment of urothelial carcinoma, a type of cancer in the bladder and urinary tract, and which includes tumors derived from a cancer of the renal pelvis. IMFINZI is specifically indicated for patients who have disease progression during or following platinum-containing chemotherapy. The medication guide included with IMFINZI's prescribing information from 2017 to 2021 and current instructions informs patients that IMFINZI may be used when the patient has tried chemotherapy that contains platinum and it did not work or is no longer working.

132. As described above, and according to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks for the treatment of urothelial carcinoma. The clinical study described in IMFINZI's prescribing information explained that 17% of patients responded to treatment.

133. On information and belief, IMFINZI has been used according to the instructions in its prescribing information from 2017 to 2021 and current instructions. The use of IMFINZI according to the instructions in its prescribing information from 2017 to 2021 and current instructions infringes at least claims 1 and 28 of the '594 patent.

134. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered for locally advanced or metastatic urothelial carcinoma. The use of IMFINZI according to its prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 2-4 and 29 of the '594 patent.

135. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to the prescribing information therefore infringes at least claims 6-9 of the ’594 patent.

136. According to IMFINZI’s prescribing information from 2017 to 2021 and current instructions, PD-L1 can be expressed on both tumor cells and tumor-associated cells in the tumor microenvironment. In the urothelial carcinoma clinical study reported in the prescribing information, more than half of the patients were classified as “PD-L1 high.” If immune cells involved greater than 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or immune cells expressed PD-L1. If immune cells involved less than or equal to 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or 100% of immune cells expressed PD-L1. IMFINZI’s prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient when at least 1% (claim 10) or 5% (claim 11) of the tumor cells exhibit membrane PD-L1 expression. Accordingly, use of IMFINZI to treat patients where at least 1% or at least 5% of the tumor cells exhibit membrane PD-L1 expression according to the prescribing information from 2017 to 2021 and current instructions infringes at least claims 10-11 and 30 of the ’594 patent.

137. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered to adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy. The clinical study reported in the prescribing information explained that 70% of patients had received prior cisplatin therapy, 30% had received prior carboplatin therapy, and 35% had received greater than or equal to 2 prior lines of systemic therapy. Based on the clinical study presented in the prescribing information, IMFINZI's prescribing information instructs doctors to use IMFINZI to treat a patient where the platinum-based chemotherapy is cisplatin, carboplatin, or both cisplatin and carboplatin. IMFINZI's prescribing information thus instructs doctors to use IMFINZI to treat a patient where the patient's tumor is refractory to cisplatin, carboplatin, or both cisplatin and carboplatin. The use of IMFINZI to treat such patients according to IMFINZI's prescribing information from 2017 to 2021 and current instructions, infringes at least claim 23 of the '594 patent.

138. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, if patients experience certain adverse reactions from taking IMFINZI, their dose can be modified. Specifically, the prescribing information instructs the doctor to administer various corticosteroid treatments depending on the adverse reaction. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claim 24 of the '594 patent.

139. On information and belief, AstraZeneca has known about the '594 patent since as early as April 23, 2019, when the '594 patent issued, but in any event, at least before receiving a copy of this complaint.

140. AstraZeneca has had knowledge of the ’594 patent since the ’594 patent issued because International Publication No. WO2013/173223 (International Application No. PCT/US2013/040764), which claims priority to the same provisional applications as the ’594 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca’s own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the ’594 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody and claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 (“the ’040 patent”), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the ’040 patent at the United States Patent & Trademark Office is “AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606.” On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune’s GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

141. Moreover, AstraZeneca has had knowledge of the ’594 patent since the ’594 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-

L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

142. AstraZeneca has had knowledge of the '594 patent since the '594 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '594 patent at that point. Therefore, AstraZeneca would have had knowledge of the '594 patent since at least that time. AstraZeneca also has had knowledge of the '594 patent since the '594 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was

later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

143. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '594 patent since the '594 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the '594 patent existed.

144. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the

use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’594 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’594 patent. If AstraZeneca did not have actual knowledge of the existence of the ’594 patent, it is because AstraZeneca was willfully blind to the existence of the ’594 patent.

145. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’594 patent since as early as April 23, 2019, when the ’594 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the ’594 patent are found directly in IMFINZI’s prescribing information. Accordingly, once AstraZeneca knew of the ’594 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the ’594 patent.

146. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’594 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’594 patent or was willfully blind to the existence of the ’594 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI’s prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the ’594 patent. Based on the similarity between the ’594 patent’s claims and IMFINZI’s prescribing

information, the only way that AstraZeneca would not know that the use of IMFINZI infringed the ’594 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’594 patent.

147. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-4, 6-11, 23-24, and 28-30 of the ’594 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’594 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’594 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’594 patent.

148. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’594 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the ’594 patent.

The Use of IMFINZI Infringes the ’595 Patent

149. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be prescribed and used for the treatment of urothelial carcinoma, including tumors derived from a cancer of the ureter, according to IMFINZI’s prescribing information from 2017 to 2021 and according to AstraZeneca’s instructions on its website even after the prescribing information was adjusted in 2021, as described above.

150. As described above, and according to prescribing information for IMFINZI from 2017 to 2021 and current instructions, IMFINZI is an anti-PD-L1 antibody used for treating a tumor in a subject in need of treatment. IMFINZI was specifically indicated for the treatment of urothelial carcinoma, a type of cancer in the bladder and urinary tract, and which includes tumors derived from a cancer of the ureter. IMFINZI is specifically indicated for patients who have disease progression during or following platinum-containing chemotherapy. The medication guide included with IMFINZI's prescribing information from 2017 to 2021 and current instructions informs patients that IMFINZI may be used when the patient has tried chemotherapy that contains platinum and it did not work or is no longer working.

151. As described above, and according to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks for the treatment of urothelial carcinoma. The clinical study described in IMFINZI's prescribing information explained that 17% of patients responded to treatment.

152. On information and belief, IMFINZI has been used according to the instructions in its prescribing information from 2017 to 2021 and current instructions. The use of IMFINZI according to the instructions in its prescribing information from 2017 to 2021 and current instructions infringes at least claims 1 and 28 of the '595 patent.

153. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered for locally advanced or metastatic urothelial carcinoma. The use of IMFINZI according to its prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 2-4 and 29 of the '595 patent.

154. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 6-9 of the ’595 patent.

155. According to IMFINZI’s prescribing information from 2017 to 2021 and current instructions, PD-L1 can be expressed on both tumor cells and tumor-associated cells in the tumor microenvironment. In the urothelial carcinoma clinical study reported in IMFINZI’s prescribing information, more than half of the patients were classified as “PD-L1 high.” If immune cells involved greater than 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or immune cells expressed PD-L1. If immune cells involved less than or equal to 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or 100% of immune cells expressed PD-L1. IMFINZI’s prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient when at least 1% (claim 10) or 5% (claim 11) of the tumor cells exhibit membrane PD-L1 expression. Accordingly, use of IMFINZI to treat patients where at least 1% or at least 5% of the tumor cells exhibit membrane PD-L1 expression according to the prescribing information infringes at least claims 10-11 and 30 of the ’595 patent.

156. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered to adult patients with locally advanced or

metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy. The clinical study reported in the prescribing information explained that 70% of patients had received prior cisplatin therapy, 30% had received prior carboplatin therapy, and 35% had received greater than or equal to 2 prior lines of systemic therapy. Based on the clinical study presented in the prescribing information, IMFINZI's prescribing information instructs doctors to use IMFINZI to treat a patient where the platinum-based chemotherapy is cisplatin, carboplatin, or both cisplatin and carboplatin. IMFINZI's prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient where the patient's tumor is refractory to cisplatin, carboplatin, or both cisplatin and carboplatin. The use of IMFINZI to treat such patients according to IMFINZI's prescribing information from 2017 to 2021 and current instructions, infringes at least claim 23 of the '595 patent.

157. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, if patients experience certain adverse reactions from taking IMFINZI, their dose can be modified. Specifically, the prescribing information instructs the doctor to administer various corticosteroid treatments depending on the adverse reaction. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claim 24 of the '595 patent.

158. On information and belief, AstraZeneca has known about the '595 patent since as early as April 23, 2019, when the '595 patent issued, but in any event, at least before receiving a copy of this complaint.

159. AstraZeneca has had knowledge of the '595 patent since the '595 patent issued because International Publication No. WO2013/173223 (International Application No.

PCT/US2013/040764), which claims priority to the same provisional applications as the ’595 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca’s own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the ’595 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody and claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 (“the ’040 patent”), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the ’040 patent at the United States Patent & Trademark Office is “AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606.” On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune’s GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

160. Moreover, AstraZeneca has had knowledge of the ’595 patent since the ’595 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name

OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

161. AstraZeneca has had knowledge of the '595 patent since the '595 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '595 patent at that point. Therefore, AstraZeneca would have had knowledge of the '595 patent since at least that time. AstraZeneca also has had knowledge of the '595 patent since the '595 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

162. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the ’595 patent since the ’595 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca’s subsidiary MedImmune, the company primarily responsible for AstraZeneca’s development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the ’040 patent, that cover the use of IMFINZI. “AstraZeneca” is listed in the correspondence address for the ’040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2017 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the ’595 patent existed.

163. AstraZeneca’s subsidiary MedImmune, the company primarily responsible for AstraZeneca’s development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the ’040 patent, that cover the use of IMFINZI. “AstraZeneca” is listed in the correspondence address for the ’040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of

IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’595 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’595 patent. If AstraZeneca did not have actual knowledge of the existence of the ’595 patent, it is because AstraZeneca was willfully blind to the existence of the ’595 patent.

164. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’595 patent since as early as April 23, 2019, when the ’595 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the ’595 patent are found directly in IMFINZI’s prescribing information. Accordingly, once AstraZeneca knew of the ’595 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the ’595 patent.

165. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’595 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’595 patent or was willfully blind to the existence of the ’595 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI’s prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the ’595 patent. Based on the similarity between the ’595 patent’s claims and IMFINZI’s prescribing information, the only way that AstraZeneca would not know that the use of IMFINZI infringed

the ’595 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’595 patent.

166. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-4, 6-11, 23-24, and 28-30 of the ’595 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’595 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’595 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’595 patent.

167. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’595 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the ’595 patent.

The Use of IMFINZI Infringes the ’596 Patent

168. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be prescribed and used for the treatment of urothelial carcinoma, including tumors derived from a cancer of the urethra, according to IMFINZI’s prescribing information from 2017 to 2021 and according to AstraZeneca’s instructions on its website even after the prescribing information was adjusted in 2021, as described above.

169. As described above, and according to prescribing information for IMFINZI from 2017 to 2021 and current instructions, IMFINZI is an anti-PD-L1 antibody used for treating a tumor in a subject in need of treatment. IMFINZI was specifically indicated for the treatment of urothelial carcinoma, a type of cancer in the bladder and urinary tract, and which includes tumors derived from a cancer of the urethra. IMFINZI is specifically indicated for patients who have disease progression during or following platinum-containing chemotherapy. The medication guide included with IMFINZI's prescribing information from 2017 to 2021 and current instructions informs patients that IMFINZI may be used when the patient has tried chemotherapy that contains platinum and it did not work or is no longer working.

170. As described above, and according to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks for the treatment of urothelial carcinoma. The clinical study described in IMFINZI's prescribing information explained that 17% of patients responded to treatment.

171. On information and belief, IMFINZI has been used according to the instructions in its prescribing information from 2017 to 2021 and current instructions. The use of IMFINZI according to the instructions in its prescribing information from 2017 to 2021 and current instructions infringes at least claims 1 and 28 of the '596 patent.

172. According to its prescribing information, IMFINZI was and is administered for locally advanced or metastatic urothelial carcinoma. The use of IMFINZI according to its prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 2-4 and 29 of the '596 patent.

173. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claims 6-9 of the ’596 patent.

174. According to IMFINZI’s prescribing information from 2017 to 2021 and current instructions, PD-L1 can be expressed on both tumor cells and tumor-associated cells in the tumor microenvironment. In the urothelial carcinoma clinical study reported in the prescribing information, more than half of the patients were classified as “PD-L1 high.” If immune cells involved greater than 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or immune cells expressed PD-L1. If immune cells involved less than or equal to 1% of the tumor area, the patient was classified as “PD-L1 high” when greater than or equal to 25% of the tumor cells or 100% of immune cells expressed PD-L1. IMFINZI’s prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient when at least 1% (claim 10) or 5% (claim 11) of the tumor cells exhibit membrane PD-L1 expression. Accordingly, use of IMFINZI to treat patients where at least 1% or at least 5% of the tumor cells exhibit membrane PD-L1 expression according to the prescribing information from 2017 to 2021 and current instructions infringes at least claims 10-11 and 30 of the ’596 patent.

175. According to its prescribing information from 2017 to 2021 and current instructions, IMFINZI was and is administered to adult patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy. The clinical study reported in the prescribing information explained that 70% of patients had received prior cisplatin therapy, 30% had received prior carboplatin therapy, and 35% had received greater than or equal to 2 prior lines of systemic therapy. Based on the clinical study presented in the prescribing information, IMFINZI's prescribing information from 2017 to 2021 and current instructions instructs doctors to use IMFINZI to treat a patient where the platinum-based chemotherapy is cisplatin, carboplatin, or both cisplatin and carboplatin. IMFINZI's prescribing information from 2017 to 2021 and current instructions thus instructs doctors to use IMFINZI to treat a patient where the patient's tumor is refractory to cisplatin, carboplatin, or both cisplatin and carboplatin. The use of IMFINZI to treat such patients according to IMFINZI's prescribing information from 2017 to 2021 and current instructions, infringes at least claim 23 of the '596 patent.

176. According to IMFINZI's prescribing information from 2017 to 2021 and current instructions, if patients experience certain adverse reactions from taking IMFINZI, their dose can be modified. Specifically, the prescribing information instructs the doctor to administer various corticosteroid treatments depending on the adverse reaction. The use of IMFINZI according to the prescribing information from 2017 to 2021 and current instructions therefore infringes at least claim 24 of the '596 patent.

177. On information and belief, AstraZeneca has known about the '596 patent since as early as April 23, 2019, when the '596 patent issued, but in any event, at least before receiving a copy of this complaint.

178. AstraZeneca has had knowledge of the ’596 patent since the ’596 patent issued because International Publication No. WO2013/173223 (International Application No. PCT/US2013/040764), which claims priority to the same provisional applications as the ’596 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca’s own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the ’596 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody and claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 (“the ’040 patent”), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the ’040 patent at the United States Patent & Trademark Office is “AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606.” On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune’s GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

179. Moreover, AstraZeneca has had knowledge of the ’596 patent since the ’596 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-

L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

180. AstraZeneca has had knowledge of the '596 patent since the '596 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '595 patent at that point. Therefore, AstraZeneca would have had knowledge of the '595 patent since at least that time. AstraZeneca also has had knowledge of the '596 patent since the '596 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was

later approved to treat. By December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

181. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '596 patent since the '596 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2017 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the '596 patent existed.

182. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the

use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’596 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’596 patent. If AstraZeneca did not have actual knowledge of the existence of the ’596 patent, it is because AstraZeneca was willfully blind to the existence of the ’596 patent.

183. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’596 patent since as early as April 23, 2019, when the ’596 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the ’596 patent are found directly in IMFINZI’s prescribing information. Accordingly, once AstraZeneca knew of the ’596 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the ’596 patent.

184. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1-4, 6-11, 23-24, and 28-30 of the ’596 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’596 patent or was willfully blind to the existence of the ’596 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI’s prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the ’596 patent. Based on the similarity between the ’596 patent’s claims and IMFINZI’s prescribing

information, the only way that AstraZeneca would not know that the use of IMFINZI infringed the ’596 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’596 patent.

185. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1-4, 6-11, 23-24, and 28-30 of the ’596 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’596 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’596 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’596 patent.

186. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’596 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the ’596 patent.

The Use of IMFINZI Infringes the ’092 Patent

187. On information and belief, AstraZeneca has manufactured, distributed, used, offered for sale, sold, and/or imported in the United States the IMFINZI antibody product to be prescribed and used for the treatment of late stage non-small cell lung cancer according to IMFINZI’s prescribing information.

188. As described above, and according to prescribing information for IMFINZI, IMFINZI is an anti-PD-L1 antibody used for treating a late-stage non-small cell lung cancer

tumor in a subject where the subject is pretreated for a chemotherapy and a radiotherapy. Specifically, according to IMFINZI's prescribing information, it is indicated for the treatment of unresectable Stage III non-small cell lung cancer whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

189. As described above, and according to IMFINZI's prescribing information, IMFINZI is indicated for administration as an intravenous infusion over 60 minutes with a recommended dosage of 10 mg/kg every 2 weeks.

190. AstraZeneca is aware that IMFINZI is used, and instructs that IMFINZI be used, to treat unresectable Stage III non-small cell lung cancers where at least 1% of tumor cells in the tumor exhibit membrane PD-L1 expression. According to IMFINZI's prescribing information, expression of PD-L1 can be induced by inflammatory signals such as Interferon-gamma and can be expressed on both tumor cells and tumor-associated immune cells in the tumor microenvironment. AstraZeneca has funded and AstraZeneca authors contributed to reports of clinical study data showing that patients with NSCLC having tumors that express PD-L1 on ≥1% of tumor cells were to be treated with IMFINZI (https://doi.org/10.1016/j.annonc.2020.03.287). Treatment with IMFINZI improved overall survival outcomes for patients having tumors that express PD-L1 on ≥1% of tumor cells (https://doi.org/10.1016/j.annonc.2020.03.287). Patients with tumors where at least 1% of tumor cells express PD-L1 are known by AstraZeneca to be treated with IMFINZI. AstraZeneca thus instructs doctors to use IMFINZI to treat a patient when at least 1% of the tumor cells exhibit membrane PD-L1 expression.

191. On information and belief, IMFINZI has been used according to the instructions in its prescribing information. The use of IMFINZI according to the instructions in its prescribing information infringes at least claim 1 of the '092 patent.

192. According to IMFINZI's prescribing information, IMFINZI is indicated for the treatment of unresectable Stage III non-small cell lung cancer. Stage III non-small cell lung cancers include cancers that are advanced, recurrent, and/or metastatic. Stage III non-small cell lung cancers include cancers that occur after the subject has had a stage I or stage II tumor surgically removed. Accordingly, the use of IMFINZI according to the instructions in its prescribing information infringes at least claims 3-5 of the '092 patent.

193. According to IMFINZI's prescribing information, IMFINZI is indicated for the treatment of unresectable Stage III non-small cell lung cancer at a dosage of 10 mg/kg every 2 weeks until disease progression, unacceptable toxicity, or a maximum of 12 months. IMFINZI's prescribing information thus instructs doctors to administer IMFINZI for up to 12 months, which is more than 12 weeks. Accordingly, the use of IMFINZI according to the instructions in its prescribing information infringes at least claim 6 of the '092 patent.

194. According to its prescribing information, IMFINZI is packaged as a 500 mg/10mL solution in a single-dose vial or as a 120 mg/2.4mL solution in a single-dose vial. Each vial contains durvalumab (IMFINZI), L-histidine, L-histidine hydrochloride monohydrate, α,α trehalose dehydrate, Polysorbate 80, and water for injection. To prepare IMFINZI for administration to a human subject, the packaged solution is transferred to an intravenous bag containing 0.9% sodium chloride or 5% dextrose. The use of IMFINZI according to the prescribing information therefore infringes at least claims 7-11 of the '092 patent.

195. On information and belief, AstraZeneca has known about the '092 patent since as early as June 18, 2019, when the '092 patent issued, but in any event, at least before receiving a copy of this complaint.

196. AstraZeneca has had knowledge of the ’092 patent since the ’092 patent issued because International Publication No. WO2013/173223 (International Application No. PCT/US2013/040764), which claims priority to the same provisional applications as the ’092 patent and identifies the same inventors, was identified during prosecution of several of AstraZeneca’s own patents. WO2013/173223 includes claims with limitations that are very similar to limitations in the claims of the ’092 patent. Claim 1 of WO2013/173223 covers a method of treating cancer by administering a PD-L1 antibody. Claim 2 identifies specific types of cancer, including non-small cell lung cancer. Claim 3 recites a dose of such an antibody from 0.1 to 10.0 mg/kg body weight at a dosing schedule of once per week, once every two weeks, or once a month. WO2013/173223 was included on a June 29, 2016 information disclosure statement during prosecution of U.S. Patent No. 10,232,040 (“the ’040 patent”), which covers certain uses of durvalumab and is assigned to MedImmune, LLC, a company owned by AstraZeneca. The correspondence address associated with the ’040 patent at the United States Patent & Trademark Office is “AstraZeneca, 300 South Wacker Dr., Chicago, IL, 60606.” On information and belief, MedImmune was responsible for developing durvalumab, previously known as MEDI4736, for AstraZeneca. On January 28, 2016, WO2013/173223 was also identified by the examiner as relevant to all claims in MedImmune’s GB2531094 publication, a publication of another application that claims uses of durvalumab. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca’s product IMFINZI.

197. Moreover, AstraZeneca has had knowledge of the ’092 patent since the ’092 patent issued because AstraZeneca and Plaintiffs are direct competitors in the immunotherapy field, and more specifically, in the PD-1/PD-L1 antibody field. AstraZeneca markets its anti-PD-

L1 antibody durvalumab under the name IMFINZI for the treatment of urothelial carcinoma and non-small cell lung cancer. Plaintiffs market the anti-PD-1 antibody nivolumab under the name OPDIVO for treating those same types of cancer. On information and belief, AstraZeneca began marketing IMFINZI on May 1, 2017. On information and belief, AstraZeneca has invested millions of dollars to develop and market IMFINZI and actively monitors its competitors' patent portfolios that could cover the IMFINZI product.

198. AstraZeneca has had knowledge of the '092 patent since the '092 patent issued because it is a large company that monitors its competitors' patent portfolios for patents that cover IMFINZI. On information and belief, it monitored Plaintiffs' patent portfolio because in or around May 2019, AstraZeneca approached Plaintiffs about licensing one or more patents in Plaintiffs' PD-L1 patent portfolio. On information and belief, at least in connection with that outreach by AstraZeneca to Plaintiffs to license Plaintiffs' PD-L1 patent portfolio, AstraZeneca investigated Plaintiffs' portfolio of PD-L1-related patents and patent applications, which included the '092 patent's family at that point, and the '092 patent when it issued shortly thereafter. Therefore, AstraZeneca would have had knowledge of the '092 patent since at least that time. AstraZeneca also has had knowledge of the '092 patent since the '092 patent issued because AstraZeneca was aware of other companies that licensed Plaintiffs' PD-L1 patent estate so those companies could sell PD-L1 antibodies. By December of 2020, AstraZeneca was aware that Plaintiffs entered a non-exclusive licensing agreement with Roche covering Plaintiffs' PD-L1 estate. Roche/Genentech, one of AstraZeneca's primary PD-L1 competitors, markets the anti-PD-L1 antibody TECENTRIQ. TECENTRIQ is an anti-PD-L1 antibody that was approved for the treatment of urothelial carcinoma in 2016 and for the treatment of non-small cell lung cancer in 2017—the same types of cancers that IMFINZI was later approved to treat. By

December of 2020, Plaintiffs and AstraZeneca again discussed licensing Plaintiffs' PD-L1 patent estate.

199. In the absence of actual knowledge, AstraZeneca has at least been willfully blind to the existence of the '092 patent since the '092 patent issued. AstraZeneca has invested millions of dollars in developing and marketing IMFINZI and owns or controls numerous patents covering IMFINZI. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca knew that Plaintiffs owned or licensed patents covering anti-PD-L1 antibodies, and their use, since at least 2019 based on previous licensing discussions between the parties. AstraZeneca knew that Plaintiffs licensed their PD-L1 estate to other companies that also market anti-PD-L1 antibodies to treat urothelial carcinoma and non-small cell lung cancer. AstraZeneca subjectively believed there was a high probability that the '092 patent existed.

200. AstraZeneca's subsidiary MedImmune, the company primarily responsible for AstraZeneca's development of IMFINZI, cited the related WO2013/173223 International Application in its own patent filings, including the '040 patent, that cover the use of IMFINZI. "AstraZeneca" is listed in the correspondence address for the '040 patent. On information and belief, AstraZeneca was aware of the MedImmune patent applications, and the citations to the BMS patents, because, for example, they related to AstraZeneca's product IMFINZI. AstraZeneca also had knowledge of other patents owned/licensed by Plaintiffs that related to the

use of an anti-PD-L1 antibody. AstraZeneca is a sophisticated company and, on information and belief, monitors the patent estates of its competitors for patents that could cover the use of IMFINZI, particularly competitors, like Plaintiffs, who AstraZeneca has approached about licensing patents that cover IMFINZI. If AstraZeneca did not have actual knowledge of the ’092 patent, it is because AstraZeneca took deliberate actions to avoid learning specifically about the ’092 patent. If AstraZeneca did not have actual knowledge of the existence of the ’092 patent, it is because AstraZeneca was willfully blind to the existence of the ’092 patent.

201. AstraZeneca has known that the use of IMFINZI in patients to treat cancer infringes at least claims 1 and 3-11 of the ’092 patent since as early as June 18, 2019, when the ’092 patent issued, but in any event, before receiving a copy of this complaint. IMFINZI is sold in a highly regulated market and AstraZeneca provided detailed prescribing information to users about how to administer and use IMFINZI. As detailed above, the limitations of the claims of the ’092 patent are found directly in IMFINZI’s prescribing information and within published articles that AstraZeneca funded and that AstraZeneca authors contributed to. Accordingly, once AstraZeneca knew of the ’092 patent, AstraZeneca knew that the use of IMFINZI according to its prescribing information would infringe the ’092 patent.

202. If AstraZeneca did not have actual knowledge that the use of IMFINZI in patients to treat cancer infringes at least claims 1 and 3-11 of the ’092 patent, then AstraZeneca was willfully blind to that fact. AstraZeneca had actual knowledge of the ’092 patent or was willfully blind to the existence of the ’092 patent. AstraZeneca is a sophisticated company and upon learning of a patent that covers the use of an anti-PD-L1 antibody according to the treatment regimen in IMFINZI’s prescribing information, AstraZeneca subjectively believed that there was a high probability the use of IMFINZI would infringe the ’092 patent. Based on the similarity

between the ’092 patent’s claims and IMFINZI’s prescribing information and information within published articles that AstraZeneca funded and that AstraZeneca authors contributed to, the only way that AstraZeneca would not know that the use of IMFINZI infringed the ’092 patent would be because AstraZeneca took deliberate action to avoid learning that the use of IMFINZI infringed the ’092 patent.

203. AstraZeneca has contributed, and continues to contribute, to the infringement of at least claims 1 and 3-11 of the ’092 patent. IMFINZI is, and has been, especially made to bind to human PD-L1 and have the features as claimed. Thus, IMFINZI is especially made, and has been made, for use to infringe the claims of the ’092 patent. Further, IMFINZI is only available, and has only been available, to purchase for use as a product with the claimed features and is not a staple article of commerce or suited for any substantial non-infringing use. For all of the reasons above, AstraZeneca knows, and has known since as early as the date the ’092 patent issued, that IMFINZI is and has been especially made and/or especially adapted for use in infringing the ’092 patent.

204. Through its prescribing information from 2017-2021 and promotional materials, including its websites, AstraZeneca has and continues to recommend and encourage healthcare providers to infringe the claims of the ’092 patent. AstraZeneca has had and continues to have the specific intent to infringe and actively induce others to infringe the ’092 patent.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 9,580,505

205. Plaintiffs incorporate by reference paragraphs 1-204 as if fully set forth herein.

206. On information and belief, AstraZeneca is marketing, making, using, selling, offering for sale, and/or importing IMFINZI in the United States for the treatment of cancer. On information and belief, IMFINZI is being used for the treatment of cancer in the United States.

As set forth above, AstraZeneca is thereby infringing at least claims 1-2, 4-7, 21-25, 28-32, 34, 36-39, and 41 of the ’505 patent directly under 35 U.S.C. § 271(a), by actively inducing infringement under 35 U.S.C. § 271(b), and as a contributory infringer under 35 U.S.C. § 271(c).

207. On information and belief, AstraZeneca has been aware of the ’505 patent since at least approximately February 28, 2017, when the USPTO issued the ’505 patent and AstraZeneca’s infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’505 patent.

208. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca’s infringement.

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

COUNT II: INFRINGEMENT OF U.S. PATENT NO. 9,580,507

210. Plaintiffs incorporate by reference paragraphs 1-209 as if fully set forth herein.

211. On information and belief, AstraZeneca is marketing, making, using, selling, offering for sale, and/or importing IMFINZI in the United States for the treatment of cancer. On information and belief, IMFINZI is being used for the treatment of cancer in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-7, 9, 11, 12, 15-19, 22, and 27-28 of the ’507 patent directly under 35 U.S.C. § 271(a), by actively inducing infringement under 35 U.S.C. § 271(b), and as a contributory infringer under 35 U.S.C. § 271(c).

212. On information and belief, AstraZeneca has been aware of the ’507 patent since at least approximately February 28, 2017, when the USPTO issued the ’507 patent and

AstraZeneca's infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the '507 patent.

213. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca's infringement.

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

COUNT III: INFRINGEMENT OF U.S. PATENT NO. 10,138,299

215. Plaintiffs incorporate by reference paragraphs 1-214 as if fully set forth herein.

216. On information and belief, AstraZeneca has marketed, made, used, sold, offered for sale, and/or imported IMFINZI in the United States for the treatment of urothelial carcinoma, and continues to do so. On information and belief, IMFINZI was and continues to be used for the treatment of urothelial carcinoma in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-11, and 22-23 of the '299 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).

217. On information and belief, AstraZeneca has been aware of the '299 patent since at least approximately November 27, 2018, when the USPTO issued the '299 patent and AstraZeneca's infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the '299 patent.

218. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca's infringement.

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

COUNT IV: INFRINGEMENT OF U.S. PATENT NO. 10,308,714

220. Plaintiffs incorporate by reference paragraphs 1-219 as if fully set forth herein.

221. On information and belief, AstraZeneca has marketed, made, used, sold, offered for sale, and/or imported IMFINZI in the United States for the treatment of urothelial carcinoma, and continues to do so. On information and belief, IMFINZI was and continues to be used for the treatment of urothelial carcinoma in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-4, 6-11, and 22-23 of the '714 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).

222. On information and belief, AstraZeneca has been aware of the '714 patent since at least approximately June 4, 2019, when the USPTO issued the '714 patent and AstraZeneca's infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the '714 patent.

223. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca's infringement.

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

COUNT V: INFRINGEMENT OF U.S. PATENT NO. 10,266,594

225. Plaintiffs incorporate by reference paragraphs 1-224 as if fully set forth herein.

226. On information and belief, AstraZeneca has marketed, made, used, sold, offered for sale, and/or imported IMFINZI in the United States for the treatment of urothelial carcinoma, and continues to do so. On information and belief, IMFINZI was and continues to be used for the treatment of urothelial carcinoma in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-4, 6-11, 23-24, and 28-30 of the ’594 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).

227. On information and belief, AstraZeneca has been aware of the ’594 patent since at least approximately April 23, 2019, when the USPTO issued the ’594 patent and AstraZeneca’s infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’594 patent.

228. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca’s infringement.

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

COUNT VI: INFRINGEMENT OF U.S. PATENT NO. 10,266,595

230. Plaintiffs incorporate by reference paragraphs 1-229 as if fully set forth herein.

231. On information and belief, AstraZeneca has marketed, made, used, sold, offered for sale, and/or imported IMFINZI in the United States for the treatment of urothelial carcinoma, and continues to do so. On information and belief, IMFINZI was and continues to be used for the treatment of urothelial carcinoma in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-4, 6-11, 23-24, and 28-30 of the ’595 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).

232. On information and belief, AstraZeneca has been aware of the ’595 patent since at least approximately April 23, 2019, when the USPTO issued the ’595 patent and AstraZeneca’s infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’595 patent.

233. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca’s infringement.

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

COUNT VII: INFRINGEMENT OF U.S. PATENT NO. 10,266,596

235. Plaintiffs incorporate by reference paragraphs 1-234 as if fully set forth herein.

236. On information and belief, AstraZeneca has marketed, made, used, sold, offered for sale, and/or imported IMFINZI in the United States for the treatment of urothelial carcinoma, and continues to do so. On information and belief, IMFINZI was and continues to be used for the treatment of urothelial carcinoma in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1-4, 6-11, 23-24, and 28-30 of the ’596 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).

237. On information and belief, AstraZeneca has been aware of the ’596 patent since at least approximately April 23, 2019, when the USPTO issued the ’596 patent and AstraZeneca’s

infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’596 patent.

238. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca’s infringement.

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

COUNT VIII: INFRINGEMENT OF U.S. PATENT NO. 10,323,092

240. Plaintiffs incorporate by reference paragraphs 1-239 as if fully set forth herein.

241. On information and belief, AstraZeneca is marketing, making, using, selling, offering for sale, and/or importing IMFINZI in the United States for the treatment of non-small cell lung cancer. On information and belief, IMFINZI is being used for the treatment of non-small cell lung cancer in the United States. As set forth above, AstraZeneca is thereby infringing at least claims 1, and 3-11 of the ’092 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).

242. On information and belief, AstraZeneca has been aware of the ’092 patent since at least approximately June 18, 2019, when the USPTO issued the ’092 patent and AstraZeneca’s infringement is deliberate, egregious, willful, and in reckless disregard of valid patent claims of the ’092 patent.

243. Plaintiffs have been and will continue to be injured by, and have suffered, and will continue to suffer, substantial damages, including lost profits, as a result of AstraZeneca’s infringement.

244. 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 Defendants infringe and will infringe the '505 patent;

(b) entry of a judgment that Defendants infringe and will infringe the '507 patent;

(c) entry of a judgment that Defendants infringe and will infringe the '299 patent;

(d) entry of a judgment that Defendants infringe and will infringe the '714 patent;

(e) entry of a judgment that Defendants infringe and will infringe the '594 patent;

(f) entry of a judgment that Defendants infringe and will infringe the '595 patent;

(g) entry of a judgment that Defendants infringe and will infringe the '596 patent;

(h) entry of a judgment that Defendants infringe and will infringe the '092 patent;

(i) an award of damages sufficient to compensate Plaintiffs for infringement of the '505, '507, '299, '714, '594, '595, '596, and '092 patents, together with pre- and post-judgment interest and costs as fixed by the Court as provided by 35 U.S.C. § 284;

(j) entry of an order compelling Defendants to compensate Plaintiffs for any ongoing or future infringement of the '505, '507, '299, '714, '594, '595, '596, and '092 patents, in an amount and under terms appropriate for the circumstances;

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

(l) 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

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

Dated: March 17, 2022

Respectfully submitted,

FARNAN LLP

/s/ Michael J. Farnan

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