EXHIBIT 18

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1 [pre]	Merck's Keytruda (Pembrolizumab)
A method for treating a patient having a solid tumor selected from the group consisting of endometrial cancer, small bowel cancer, gastric cancer, ampullary cancer, choloangiocarcinoma, pancreatic cancer, prostate cancer, breast cancer, esophageal cancer, liver cancer, ovarian cancer, uterine cancer, cervical cancer, bladder cancer, testicular cancer and oral cancer that has progressed following at least one prior treatment, the method comprising:	Merck's FDA-approved label for Keytruda (pembrolizumab) ("Keytruda Label") instructs physicians to use Keytruda (pembrolizumab) to treat a patient having a solid tumor selected from the group consisting of endometrial cancer, small bowel cancer, gastric cancer, ampullary cancer, cholangiocarcinoma, pancreatic cancer, prostate cancer, breast cancer, esophageal cancer, liver cancer, ovarian cancer, uterine cancer, cervical cancer, bladder cancer, testicular cancer and oral cancer that has progressed following at least one prior treatment. For example, the Indications and Usage Section of the Keytruda Label lists Indication 1.7 for the treatment of adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors that have progressed following at least one prior treatment. A physician would understand that endometrial cancer, small bowel cancer, gastric cancer, ampullary cancer, cholangiocarcinoma, pancreatic cancer, prostate cancer, breast cancer, esophageal cancer, liver cancer, ovarian cancer, uterine cancer, cervical cancer, bladder cancer, testicular cancer and oral cancer can present as an unresectable or metastatic solid tumor. **1.7 Microsatellite Instability-High or Mismatch Repair Deficient Cancer** KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options *[see Dosage and Administration (2.1)]*. Label at 5. The Indications and Usage Section of the Keytruda Label also lists Indication 1.15 for the treatment of patients with advanced endometrial carcinoma that are MSI-H or dMMR that has progressed following at least one prior treatment.

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1 [pre]	Merck's Keytruda (Pembrolizumab)
	1.15 Endometrial Carcinoma KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation *[see Dosage and Administration (2.1)]*. KEYTRUDA, as a single agent, is indicated for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation *[see Dosage and Administration (2.1)]*. Label at 6 (highlighting added).

Claim 1[a]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab
testing or having tested a biological sample obtained from the patient to determine whether the solid tumor is microsatellite instability high or DNA mismatch repair deficient; and	The Keytruda Label instructs physicians to test or have tested a biological sample obtained from a patient's solid tumor to determine whether the solid tumor is microsatellite instability high or DNA mismatch repair deficient. For example, the Keytruda Label indicates that Keytruda is approved for the treatment of patients with solid tumors that are MSI-H or dMMR as determined by an FDA-approved test: **1.7 Microsatellite Instability-High or Mismatch Repair Deficient Cancer** KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options *[see Dosage and Administration (2.1)]*. Label at 5. The Keytruda Label also indicates that Keytruda is approved for the treatment of patients with

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[a]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab
	advanced endometrial cancer that is MSI-H or dMMR as determined by an FDA-approved test: **1.15 Endometrial Carcinoma** KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation *[see Dosage and Administration (2.1)]*. KEYTRUDA, as a single agent, is indicated for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation *[see Dosage and Administration (2.1)]*. Label at 6 (highlighting added). The Dosage and Administration section of the Keytruda Label instructs physicians to test or have tested the patient's tumor specimen for MSI-H/dMMR status to select patients for single treatment with Keytruda according to Indications 1.7 and 1.15. **2 DOSAGE AND ADMINISTRATION** **2.1 Patient Selection** Patient Selection for Single-Agent Treatment Select patients for treatment with KEYTRUDA as a single agent based on the presence of positive PD-L1 expression in: • stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation *[see Clinical Studies (14.2)]*. • metastatic NSCLC *[see Clinical Studies (14.2)]*. • first-line treatment of metastatic or unresectable, recurrent HNSCC *[see Clinical Studies (14.3)]*. • previously treated recurrent locally advanced or metastatic esophageal cancer *[see Clinical Studies (14.10)]*. • recurrent or metastatic cervical cancer with disease progression on or after chemotherapy *[see Clinical Studies (14.11)]*. For the MSI-H/dMMR indications, select patients for treatment with KEYTRUDA as a single agent based on MSI-H/dMMR status in tumor specimens *[see Clinical Studies (14.7, 14.8)]*. Label at 7 (highlighting added). The Dosage and Administration section of the Keytruda Label refers physicians to a website to find

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[a]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab
	information necessary to test or have tested a biological sample obtained from a patient to determine whether the cancer is microsatellite instability high or DNA mismatch repair deficient: Additional Patient Selection Information Information on FDA-approved tests for patient selection is available at: http://www.fda.gov/CompanionDiagnostics . Label at 8. The FDA provides a List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools) which lists the diagnostic tools approved to for testing or having tested a biological sample obtained from a patient to determine whether the solid tumor is MSI-H or dMMR. Diagnostic Name (Manufacturer) | Indication - Sample Type | Drug Trade Name (Generic) NDA / BLA | Biomarker(s) | Biomarker(s) (Details) | PMA / 510(k) / 513(f)(2) / HDE (Approval / Clearance / Grant Date)

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[a]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab

FoundationOne CDx (Foundation Medicine, Inc.)	Solid Tumors - Tissue	Keytruda (pembrolizumab) BLA 125514	TMB	TMB ≥ 10 mutations per megabase	P170019/S016 (06/16/2020)
FoundationOne CDx (Foundation Medicine, Inc.)	Solid Tumors - Tissue	Keytruda (pembrolizumab) BLA 125514	MSI-High	Microsatellite instability-High (MSI-H)	P170019/S029 (02/18/2022)
PD-L1 IHC 22C3 pharmDx (Dako North America, Inc.)	Non-Small Cell Lung Cancer (NSCLC) - Tissue	Keytruda (pembrolizumab) BLA 125514	PD-L1	PD-L1 protein expression	P150013 (10/02/2015)
PD-L1 IHC 22C3 pharmDx (Dako North America, Inc.)	Cervical Cancer - Tissue	Keytruda (pembrolizumab) BLA 125514	PD-L1	PD-L1 protein expression	P150013/S009 (06/12/2018)
PD-L1 IHC 22C3 pharmDx (Dako North America, Inc.)	Head and Neck Squamous Cell Carcinoma (HNSCC) - Tissue	Keytruda (pembrolizumab) BLA 125514	PD-L1	PD-L1 protein expression	P150013/S014 (06/10/2019)
PD-L1 IHC 22C3 pharmDx (Dako North America, Inc.)	Esophageal Squamous Cell Carcinoma (ESCC) - Tissue	Keytruda (pembrolizumab) BLA 125514	PD-L1	PD-L1 protein expression	P150013/S016 (07/30/2019)
PD-L1 IHC 22C3 pharmDx (Dako North America, Inc.)	Triple-Negative Breast Cancer (TNBC) - Tissue	Keytruda (pembrolizumab) BLA 125514	PD-L1	PD-L1 protein expression	P150013/S020 (11/13/2020)
Ventana MMR RxDx Panel (Ventana Medical Systems, Inc.)	Solid Tumors	Keytruda (pembrolizumab) BLA 125514	deficient mismatch repair (dMMR) proteins	MLH1, PMS2, MSH2 and MSH6	P210001/S001 (03/21/2022)

https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools (last accessed May 16, 2023).

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[b]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab
in response to determining that the solid tumor is microsatellite instability high or DNA mismatch repair deficient, treating the patient determined to have a solid tumor that is microsatellite instability high or DNA mismatch repair deficient with a therapeutically effective amount of pembrolizumab.	The Keytruda Label instructs physicians on how to treat a patient determined to have a solid tumor selected from the group consisting of endometrial cancer, small bowel cancer, gastric cancer, ampullary cancer, cholangiocarcinoma, pancreatic cancer, prostate cancer, breast cancer, esophageal cancer, liver cancer, ovarian cancer, uterine cancer, cervical cancer, bladder cancer, testicular cancer and oral cancer that is microsatellite instability high or DNA mismatch repair deficient with a therapeutically effective amount of pembrolizumab. The Keytruda Label discloses that Keytruda is a pembrolizumab injection. **KEYTRUDA® (pembrolizumab) injection, for intravenous use** **Initial U.S. Approval: 2014** Label at 1. For, example, the Dosage and Administration section of the Keytruda Label instructs physicians to test or have tested the patient's tumor specimen for MSI-H/dMMR status to select patients for single treatment with Keytruda according to Indications 1.7 and 1.15. *See* 1[a] above. The Recommended Dosage section of the Keytruda Label provides the recommended dosages of Keytruda as well as the duration/timing of treatment by the indication, wherein the indication is directed to cancer confirmed to be MSI-high/MMR deficient.

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[b]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab

2.2 Recommended Dosage

Table 1: Recommended Dosage

Indication	Recommended Dosage of KEYTRUDA	Duration/Timing of Treatment
Monotherapy		
Adult patients with unresectable or metastatic melanoma	200 mg every 3 weeks* or 400 mg every 6 weeks*	Until disease progression or unacceptable toxicity
Adjuvant treatment of adult patients with melanoma or RCC	200 mg every 3 weeks* or 400 mg every 6 weeks*	Until disease recurrence, unacceptable toxicity, or up to 12 months
Adult patients with NSCLC, HNSCC, cHL, PMBCL, locally advanced or metastatic Urothelial Carcinoma, MSI-H or dMMR Cancer, MSI-H or dMMR CRC, MSI-H or dMMR Endometrial Carcinoma, Esophageal Cancer, Cervical Cancer, HCC, MCC, TMB-H| Cancer, or cSCC	200 mg every 3 weeks* or 400 mg every 6 weeks*	Until disease progression, unacceptable toxicity, or up to 24 months

* 30-minute intravenous infusion
† Refer to the Prescribing Information for the agents administered in combination with KEYTRUDA for recommended dosing information, as appropriate.
‡ When axitinib is used in combination with KEYTRUDA, dose escalation of axitinib above the initial 5 mg dose may be considered at intervals of six weeks or longer.
§ Patients who experience disease progression or unacceptable toxicity related to KEYTRUDA with neoadjuvant treatment in combination with chemotherapy should not receive adjuvant single agent KEYTRUDA.

Label at 8-9 (highlighting added).

The Preparation and Administration section of the Keytruda Label provides instructions for preparing and administering Keytruda to patients:

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[b]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab
	2.4 Preparation and Administration Preparation for Intravenous Infusion • Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to slightly yellow. Discard the vial if visible particles are observed. • Dilute KEYTRUDA injection (solution) prior to intravenous administration. • Withdraw the required volume from the vial(s) of KEYTRUDA and transfer into an intravenous (IV) bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. **Mix diluted solution by gentle inversion.** Do not shake. The final concentration of the diluted solution should be between 1 mg/mL to 10 mg/mL. • Discard any unused portion left in the vial. Storage of Diluted Solution The product does not contain a preservative. Store the diluted solution from the KEYTRUDA 100 mg/4 mL vial either: • At room temperature for no more than 6 hours from the time of dilution. This includes room temperature storage of the diluted solution, and the duration of infusion. • Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 96 hours from the time of dilution. If refrigerated, allow the diluted solution to come to room temperature prior to administration. Do not shake. Discard after 6 hours at room temperature or after 96 hours under refrigeration. Do not freeze. Administration • Administer diluted solution intravenously over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2 micron to 5 micron in-line or add-on filter. • Do not co-administer other drugs through the same infusion line. Label at 11. The Keytruda Label includes clinical trial results showing that the recommended dosages of Keytruda are a therapeutically effective amount among patients with MSI-H or dMMR solid tumors relevant to Indication 1.7.

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

14.7 Microsatellite Instability-High or Mismatch Repair Deficient Cancer

The efficacy of KEYTRUDA was investigated in patients with MSI-H or mismatch repair deficient (dMMR), solid tumors enrolled in one of five uncontrolled, open-label, multi-cohort, multi-center, single-arm trials. Patients with active autoimmune disease or a medical condition that required immunosuppression were ineligible across the five trials. Patients received either KEYTRUDA 200 mg every 3 weeks or KEYTRUDA 10 mg/kg every 2 weeks. Treatment continued until unacceptable toxicity or disease progression that was either symptomatic, rapidly progressive, required urgent intervention, or occurred with a decline in performance status. A maximum of 24 months of treatment with KEYTRUDA was administered. For the purpose of assessment of anti-tumor activity across these 5 trials, the major efficacy outcome measures were ORR as assessed by BICR according to RECIST v1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, and DoR.

Table 65: MSI-H Trials

Study	Design and Patient Population	Number of Patients	MSI-H/dMMR Testing	Dosage	Prior Therapy
KEYNOTE-016 NCT01876511	• prospective, investigator-initiated • 6 sites • patients with CRC and other tumors	28 CRC 30 non-CRC	local PCR or IHC	10 mg/kg every 2 weeks	• CRC: ≥ 2 prior regimens • Non-CRC: ≥1 prior regimen
KEYNOTE-164 NCT02460198	• prospective international multi-center • CRC	61	local PCR or IHC	200 mg every 3 weeks	Prior fluoropyrimidine, oxaliplatin, and irinotecan +/- anti-VEGF/EGFR mAb
KEYNOTE-012 NCT01848834	• retrospectively identified patients with PD-L1-positive gastric, bladder, or triple-negative breast cancer	6	central PCR	10 mg/kg every 2 weeks	≥1 prior regimen
KEYNOTE-028 NCT02054806	• retrospectively identified patients with PD-L1-positive esophageal, biliary, breast, endometrial, or CRC	5	central PCR	10 mg/kg every 2 weeks	≥1 prior regimen
KEYNOTE-158 NCT02628067	• prospective international multi-center enrollment of patients with MSI-H/dMMR non-CRC • retrospectively identified patients who were enrolled in specific rare tumor non-CRC cohorts	19	local PCR or IHC (central PCR for patients in rare tumor non-CRC cohorts)	200 mg every 3 weeks	≥1 prior regimen
Total		**149**			

CRC = colorectal cancer
PCR = polymerase chain reaction
IHC = immunohistochemistry

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[b]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab

Table 66: Efficacy Results for Patients with MSI-H/dMMR Cancer

Endpoint	KEYTRUDA n=149
Objective Response Rate	
ORR (95% CI)	39.6% (31.7, 47.9)
Complete response rate	7.4%
Partial response rate	32.2%
Duration of Response	
Median in months (range)	NR (1.6+, 22.7+)
% with duration ≥6 months	78%

NR = not reached

Table 67: Response by Tumor Type

	N	Objective Response Rate n (%)	95% CI	Duration of Response range (months)
CRC	90	32 (36%)	(26%, 46%)	(1.6+, 22.7+)
Non-CRC	59	27 (46%)	(33%, 59%)	(1.9+, 22.1+)
Endometrial cancer	14	5 (36%)	(13%, 65%)	(4.2+, 17.3+)
Biliary cancer	11	3 (27%)	(6%, 61%)	(11.6+, 19.6+)
Gastric or GE junction cancer	9	5 (56%)	(21%, 86%)	(5.8+, 22.1+)
Pancreatic cancer	6	5 (83%)	(36%, 100%)	(2.6+, 9.2+)
Small intestinal cancer	8	3 (38%)	(9%, 76%)	(1.9+, 9.1+)
Breast cancer	2	PR, PR		(7.6, 15.9)
Prostate cancer	2	PR, SD		9.8+
Bladder cancer	1	NE		
Esophageal cancer	1	PR		18.2+
Sarcoma	1	PD		
Thyroid cancer	1	NE		
Retroperitoneal adenocarcinoma	1	PR		7.5+
Small cell lung cancer	1	CR		8.9+
Renal cell cancer	1	PD		

CR = complete response
PR = partial response
SD = stable disease
PD = progressive disease
NE = not evaluable

Label at 89-90 (highlighting added).

The Keytruda Label also includes clinical trial results showing that the recommended dosages of Keytruda are a therapeutically effective amount of pembrolizumab among patients with MSI-H or dMMR endometrial tumors relevant to Indication 1.15.

14.15 Endometrial Carcinoma

EXHIBIT 18: INFRINGEMENT OF U.S. PATENT NO. 11,643,462 BY KEYTRUDA

Claim 1[b]	Merck Induces Infringement of JHU's Methods for Treating With Pembrolizumab

As a Single Agent for the Treatment of Advanced MSI-H or dMMR Endometrial Carcinoma

The efficacy of KEYTRUDA was investigated in KEYNOTE-158 (NCT02628067), a multicenter, non-randomized, open-label, multi-cohort trial. The trial enrolled 90 patients with unresectable or metastatic MSI-H or dMMR endometrial carcinoma in Cohorts D and K who received at least one dose of KEYTRUDA. MSI or MMR tumor status was determined using polymerase chain reaction (PCR) or immunohistochemistry (IHC), respectively. Patients with autoimmune disease or a medical condition that required immunosuppression were ineligible. Patients received KEYTRUDA 200 mg intravenously every 3 weeks until unacceptable toxicity or documented disease progression. Patients treated with KEYTRUDA without disease progression could be treated for up to 24 months. Assessment of tumor status was performed every 9 weeks for the first 12 months, and every 12 weeks thereafter. The major efficacy outcome measures were ORR and DoR as assessed by BICR according to RECIST v1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ.

Among the 90 patients evaluated, the baseline characteristics were: median age of 64 years (range: 42 to 86); 83% White, 8% Asian, and 3% Black; 12% Hispanic or Latino; 39% ECOG PS of 0 and 61% ECOG PS of 1; 96% had M1 disease and 4% had M0 disease at study entry; and 51% had one and 48% had two or more prior lines of therapy. Nine patients received only adjuvant therapy and one patient received only neoadjuvant and adjuvant therapy before participating in the study.

Efficacy results are summarized in Table 80.

Table 80: Efficacy Results in Patients with Advanced MSI-H or dMMR Endometrial Carcinoma in KEYNOTE-158

Endpoint	KEYTRUDA n=90*
Objective Response Rate	
ORR (95% CI)	46% (35, 56)
Complete response rate	12%
Partial response rate	33%
Duration of Response	n=41
Median in months (range)	NR (2.9, 55.7+)
% with duration ≥12 months	68%
% with duration ≥24 months	44%

* Median follow-up time of 16.0 months (range 0.5 to 62.1 months)
\+ Denotes ongoing response
NR = not reached

Label at 111, 114-115 (highlighting added).