UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC,
Petitioner,

v.

THE JOHNS HOPKINS UNIVERSITY,
Patent Owner.

Case IPR2024-00648
Patent 11,643,462 B2

PATENT OWNER'S UNOPPOSED MOTION FOR *PRO HAC VICE* ADMISSION OF CAROLINE (GRACIE) KOONCE UNDER 37 C.F.R. § 42.10(c)

PATENT OWNER'S UPDATED EXHIBIT LIST

Exhibit Number	Description
2001	RESERVED
2002	Curriculum Vitae of Dr. Nils Lonberg
2003	Dung T. Le, Sidney Kimmel Comprehensive Cancer Center, PD-1 Blockade in Tumors with Mismatch Repair Deficiency, Presentation at 2015 ASCO Annual Meeting (May 30, 2015) (abstract available at https://meetings.asco.org/abstracts-presentations/109904)
2004	FDA News Release, FDA, FDA Approves First Cancer Treatment for Any Solid Tumor with a Specific Genetic Feature (May 23, 2017) available at https://www.fda.gov/news-events/press-announcements/fda-approves-first-cancer-treatment-any-solid-tumor-specific-genetic-feature
2005	Gina Kolata, Cancer Drug Proves to Be Effective Against Multiple Tumors, N.Y. Times (June 8, 2017), https://www.nytimes.com/2017/06/08/health/cancer-drug-keytruda-tumors.html
2006	Laurie McGinley, 'This is not the end': Using immunotherapy and a genetic glitch to give cancer patients hope, Wash. Post (May 28, 2017), https://www.washingtonpost.com/national/health-science/this-is-not-the-end-experimental-therapy-that-targets-genes-gives-cancer-patients-hope/2017/05/28/cdce31de-365c-11e7-b373-418f6849a004_story.html
2007	News Release, Merck, Merck Receives Accelerated Approval of KEYTRUDA® (Pembrolizumab), the First FDA-Approved Anti-PD-1 Therapy (Sept. 4, 2014) available at https://www.merck.com/news/merck-receives-accelerated-approval-of-keytruda-pembrolizumab-the-first-fda-approved-anti-pd-1-therapy/
2008	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2023 Financial Results (Feb. 1, 2024) available at https://s2.q4cdn.com/584635680/files/doc_news/Merck-Announces-Fourth-Quarter-and-Full-Year-2023-Financial-Results-2024.pdf
2009-2021	RESERVED

Exhibit Number	Description
2022	Bacher et al., Development of a Fluorescent Multiplex Assay for Detection of MSI-High Tumors, 20(4-5) Disease Markers 237-50 (2004)
2023	Diaz et al., Liquid Biopsies: Genotyping Circulating Tumor DNA, 32(6) J. Clinical Oncology 579-86 (Feb. 20, 2014)
2024	Brahmer et al., Phase I Study of Single-Agent Anti–Programmed Death-1 (MDX-1106) in Refractory Solid Tumors: Safety, Clinical Activity, Pharmacodynamics, and Immunologic Correlates, 28(19) J. Clinical Oncology 3167-75 (July 1, 2010)
2025	The Cancer Genome Atlas Network, Comprehensive Molecular Characterization of Human Colon and Rectal Cancer, 487 Nature 330-37 (July 19, 2012)
2026	Mandrekar et al., All-Comers versus Enrichment Design Strategy in Phase II Trials, 6(4) J. Thoracic Oncology 658-60 (Apr. 1, 2011)
2027	Freidlin et al., Randomized Clinical Trials With Biomarkers: Design Issues, 102(3) J. Nat'l Cancer Inst. 152-60 (Feb. 3, 2010)
2028	Malik et al., Consensus Report of a Joint NCI Thoracic Malignancies Steering Committee: FDA Workshop on Strategies for Integrating Biomarkers into Clinical Development of New Therapies for Lung Cancer Leading to the Inception of "Master Protocols" in Lung Cancer, 9(10) J. Thoracic Oncology 1443-48 (Oct. 2014)
2029-2031	RESERVED
2032	NIH National Cancer Institute, What is Cancer? (last updated Oct. 11, 2021), https://www.cancer.gov/about-cancer/understanding/what-is-cancer
2033	Weiss, Open Questions: Knowing Who's Who in Multicellular Animals is Not Always as Simple as We Imagine, 16 BMC Biology Article number: 115 (Oct. 15, 2018)
2034	Mumphrey et al., Distinct Mutational Processes Shape Selection of MHC Class I and Class II Mutations Across Primary and Metastatic Tumors, 42(8) Cell Reports 112965 1-20 (Aug. 29, 2023)
2035	Jenkins et al., Antigen Presentation by Chemically Modified Splenocytes Induces Antigen-Specific T Cell Unresponsiveness In Vitro and In Vivo, 165(2) J. Experimental Med. 302-19 (Feb. 1, 1987)

Exhibit Number	Description
2036	Wherry et al., Viral Persistence Alters CD8 T-Cell Immunodominance and Tissue Distribution and Results in Distinct Stages of Functional Impairment, 77(8) J. Virology 4911-27 (Apr. 2003)
2037	Lotze et al., Lysis of Fresh and Cultured Autologous Tumor by Human Lymphocytes Cultured in T-Cell Growth Factor, 41 Cancer Research 4420-25 (Nov. 1981)
2038	Briukhovetska et al., Interleukins in Cancer: From Biology to Therapy, 21 Nature Reviews Cancer 481-99 (June 3, 2021)
2039	Bod et al., B-Cell-Specific Checkpoint Molecules That Regulate Anti-Tumour Immunity, 619 Nature 348-56 (June 21, 2023)
2040	Wang et al., CD19+CD24hiCD38hiBregs Involved in Downregulate Helper T Cells and Upregulate Regulatory T Cells in Gastric Cancer, 6(32) Oncotarget 33486-99 (Sept. 10, 2015)
2041	Michaud et al., Regulatory B Cells in Cancer, 299(1) Immunological Reviews 74-92 (Dec. 23, 2020)
2042	Nakhoda et al., Addressing Recent Failures in Immuno-Oncology Trials to Guide Novel Immunotherapeutic Treatment Strategies, 34 Pharmaceutical Medicine 83-91 (Mar. 10, 2020)
2043	Korman et al., The Foundations of Immune Checkpoint Blockade and the Ipilimumab Approval Decennial, 21 Nature Reviews Drug Discovery 509-28 (July 2022)
2044	NIH National Cancer Institute, Immune Checkpoint Inhibitors (last updated Apr. 7, 2022), https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors
2045	Boland et al., Microsatellite Instability in Colorectal Cancer, 138(6) Gastroenterology 2073-87 (May 2010)
2046	Branch et al., Immune Surveillance in Colorectal Carcinoma, 9 Nature Genetics 231-32 (Mar. 1995)
2047	Kloor et al., Immune Evasion of Microsatellite Unstable Colorectal Cancers, 127(5) Int'l J. Cancer 1001-10 (Sept. 1, 2010)
2048	Zhong et al., Comparison of the Molecular and Cellular Phenotypes of Common Mouse Syngeneic Models with Human Tumors, 21 BMC Genomics Article number: 2 (Jan. 2, 2020)
2049	Thomas et al., Advancing Translational Research for Colorectal Immuno-Oncology, 129 British J. Cancer 1442-50 (Aug. 10, 2023)

Exhibit Number	Description
2050	Lacombe et al., The Dream and Reality of Histology Agnostic Cancer Clinical Trials, 8(6) Molecular Oncology 1057-63 (Sept. 12, 2014)
2051	David Shaywitz, The Startling History Behind Merck's New Cancer Blockbuster, FORBES (July 26, 2017)
2052-2059	RESERVED
2060	News Release, Merck, FDA Approves Merck's KEYTRUDA® (pembrolizumab) for Adult and Pediatric Patients with Unresectable or Metastatic, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors (May 25, 2017)
2061	News Release, Merck, First Study Evaluating DNA Mismatch Repair as Genetic Guide for Immunotherapy Treatment with Merck's KEYTRUDA® (pembrolizumab) Presented at 2015 ASCO Annual Meeting and Published in the New England Journal of Medicine (May 29, 2015)
2062	News Release, Merck, Merck Receives Breakthrough Therapy Designation from U.S. Food and Drug Administration for KEYTRUDA® (pembrolizumab) in Advanced Colorectal Cancer (Nov. 2, 2015)
2063	Thomson Reuters Streetevents, Edited Transcript MRK - Q4 2018 Merck & Co Inc Earnings Call, event date Feb. 1, 2019
2064	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2022 Financial Results (Feb. 2, 2023)
2065	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2021 Financial Results (Feb. 3, 2022)
2066	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2020 Financial Results (Feb. 4, 2021)
2067	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2019 Financial Results (Feb. 5, 2020)
2068	News Release, Merck, Merck Announces Fourth-Quarter and Full-Year 2018 Financial Results (Feb. 1, 2019)
2069	Exhibit 18 to Johns Hopkins University Corrected Answer and Counterclaims to Complaint, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR, D.I. 17-18 (D. Md. April 21, 2023)
2070	Statista, Leading drugs worldwide based on projected 2024 sales (in billion of U.S. dollars), released December 2023, available at

Exhibit Number	Description
	https://www.statista.com/statistics/973523/top-drugs-by-year-on-year-sales-increase/
2071	Letter to Magistrate Judge Aslan from The Johns Hopkins University, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR, D.I. 100 (D. Md. May 14, 2024)
2072	Declaration of Dr. Nils Lonberg
2073	Connolly et al., Novel Mouse Models for Cancer Immunology, Annual Review of Cancer Biology 6:269-91 (2022)
2074	Sun et al., Immune checkpoint therapy for solid tumours: clinical dilemmas and future trends, Signal Transduction Targeted Therapy, 8:320 (2023)
2075	Dobosz et al., Challenges of the Immunotherapy: Perspectives and Limitations of the Immune Checkpoint Inhibitor Treatment Int. J. Mol. Sci., 23, 2847:1-17 (2022)
2076	Jonathan Gardner, Merck suffers bad week as 3 Keytruda combination trials fail, BioPharma Dive (Dec. 8, 2023), https://www.biopharmadive.com/news/merck-keytruda-combination-trials-fail-patent-cliff/701975/
2077	Angus Liu, Merck's Keytruda flunks pivotal studies in lung and skin cancers, Fierce Pharma (Aug. 29, 2024), https://www.fiercepharma.com/pharma/mercks-keytruda-flunks-early-stage-lung-and-skin-cancer-tests
2078	Jared S. Hopkins, Merck Keeps Striking Out on Expanding Its Cancer-Drug Juggernaut, The Wall Street Journal (April 26, 2023), https://www.wsj.com/articles/merck-keeps-striking-out-on-expanding-its-cancer-drug-juggernaut-637c83d4
2079	Merck's trial of Keytruda regimen fails to meet primary endpoint, Clinical Trials Arena (May 10, 2024), https://www.clinicaltrialsarena.com/news/merck-trial-keytruda-regimen/?cf-view
2080	Study of Pembrolizumab (MK-3475) in Participants With Advanced Solid Tumors (MK-3475-028/KEYNOTE-28), ClinicalTrials.gov (Oct. 10, 2023), https://clinicaltrials.gov/study/NCT02054806
2081	van der Bruggen et al., A gene encoding an antigen recognized by 7cytolytic T lymphocytes on a human melanoma, Science 254:1643-47 (Dec. 13, 1991)

Exhibit Number	Description
2082	Lawrence et al., Mutational heterogeneity in cancer and the search for new cancer-associated genes, Nature 499:214-18 (July 11, 2013)
2083	Shigehisa Kitano et al., Myeloid-derived suppressor cell quantity prior to treatment with ipilimumab at 10mg/kg to predict for overall survival in patients with metastatic melanoma, J. of Clin. Oncology 30(15), 2518 (May 20, 2012)
2084	Snyder et al., Genetic basis for clinical response to CTLA-4 blockade in melanoma, N. Engl. J. Med. 371(23):2189-99 (Dec. 4 2014)
2085	Chan et al., Genetic Basis for Clinical Response to CTLA-4 Blockade in Melanoma, N. Engl. J. Med. 373(20):1984 (Nov. 12, 2015)
2086	McGranahan et al., Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade, Science 351(6280):1463-69 (Mar. 25, 2016)
2087	Hellmann et al., Tumor Mutational Burden and Efficacy of Nivolumab Monotherapy and in Combination with Ipilimumab in Small-Cell Lung Cancer, Cancer Cell 33, 853-861 (May 14, 2018)
2088	FDA grants nivolumab accelerated approval for MSI-H or dMMR colorectal cancer, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-nivolumab-accelerated-approval-msi-h-or-dmmr-colorectal-cancer
2089	Boyiadzis et al., Significance and implications of FDA approval of pembrolizumab for biomarker-defined disease, J. ImmunoTher. Cancer 6:35 (May 14, 2018)
2090	Declaration of Dr. Richard Goldberg
2091	Bray et al., Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA Cancer J. Clin. 74:229-263 (2024)
2092	Zeineddine et al., Survival improvement for patients with metastatic colorectal cancer over twenty years, NPJ Precis. Oncol. 7:16 (2023)
2093	Patel et al., The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection, Lancet Gastroenterol Hepatol. 7: 262–74 (2022)
2094	Frank A. Sinicrope, Increasing Incidence of Early-Onset Colorectal Cancer, N. Engl. J. Med. 86:1547-58 (Apr. 21, 2022)
2095	Frank A. Sinicrope, Lynch Syndrome-Associated Colorectal Cancer, N. Engl. J. Med. 379:764-73 (Aug. 23, 2018)

Exhibit Number	Description
2096	Sargent et al., Defective mismatch repair as a predictive marker for lack of efficacy of fluorouracil-based adjuvant therapy in colon cancer, J. Clin. Oncol. 28:3219-3226 (July 10, 2010)
2097	Keung et al., The eighth edition American Joint Committee on Cancer (AJCC) melanoma staging system: implications for melanoma treatment and care, Expert Rev. Anticancer Ther. 18(8):775–784 (2018)
2098	Ogunwobi et al., Biomarkers in Colorectal Cancer: Current Research and Future Prospects, Int. J. Mol. Sci. 21, 5311 (2020)
2099	Kong et al., Prolonged surveillance of colorectal cancer patients after curative surgeries beyond five years of follow-up, Ann. Transl. Med. 7(21):608 (2019)
2100	Modulation of fluorouracil by leucovorin in patients with advanced colorectal cancer: evidence in terms of response rate, Advanced Colorectal Cancer Meta-Analysis Project 10:896:903 (1992)
2101	Dy et al., Long-term survivors of metastatic colorectal cancer treated with systemic chemotherapy alone: a North Central Cancer Treatment Group review of 3811 patients, N0144, Clin. Colorectal Cancer 8(2):88-93 (2009)
2102	Saltz et. al., Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer, Irinotecan Study Group, N. Engl. J. Med. 343(13):905-13 (2000)
2103	Sanoff et al., Five-year data and prognostic factor analysis of oxaliplatin and irinotecan combinations for advanced colorectal cancer: N9741, J. Clin. Oncol. 26:5721-5727 (2008)
2104	Hurwitz et al., Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer, N. Engl. J. Med. 350(23):35-42 (June 3, 2004)
2105	Saltz et al., Phase II trial of cetuximab in patients with refractory colorectal cancer that expresses the epidermal growth factor receptor, J. Clin. Oncol. 22:1201-1208 (Apr. 1, 2004)
2106	Van Cutsem at al., Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer, N. Engl. J. Med. 360(14):1408-17 (Apr. 2, 2009)
2107	Van Cutsem et al., Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in

Exhibit Number	Description
	patients with chemotherapy-refractory metastatic colorectal cancer, J. Clin. Oncol. 25(13):1658-64 (May 1, 2007)
2108	Tabernero et al., Aflibercept versus placebo in combination with fluorouracil, leucovorin and irinotecan in the treatment of previously treated metastatic colorectal cancer: prespecified subgroup analyses from the VELOUR trial, Eur. J. Cancer 50:320-331 (2014)
2109	Venook et al., Effect of First-Line Chemotherapy Combined With Cetuximab or Bevacizumab on Overall Survival in Patients With KRAS Wild-Type Advanced or Metastatic Colorectal Cancer: A Randomized Clinical Trial, JAMA 317(23):2392-2401 (2017)
2110	McRee at al., Optimal management of metastatic colorectal cancer: current status, Drugs 71(7):869-884 (2011)
2111	Lucas et al., A decade of advances in cytotoxic chemotherapy for metastatic colorectal cancer, Clin. Colorectal Cancer 10(4):238-44 (Dec. 2011)
2112	Modest et al., Treatment sequencing in metastatic colorectal cancer, Eur. J. Cancer 109:70-83 (2019)
2113	Grothey et al., Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicentre, randomised, placebo-controlled, phase 3 trial, Lancet 381: 303–12 (Jan. 26, 2013)
2114	Mayer et al., Randomized trial of TAS-102 for refractory metastatic colorectal cancer, N. Engl. J. Med. 372(20):1909-19 (May 14, 2015)
2115	Topalian et al., Immune checkpoint blockade: a common denominator approach to cancer therapy, Cancer Cell 27:450-61 (Apr. 13, 2015)
2116	Robert et al., Pembrolizumab versus Ipilimumab in Advanced Melanoma, N. Engl. J. Med. 372(26):2521-32 (June 25, 2015)
2117	Reck et al., Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer, N. Engl. J. Med. 375(19):1823-33 (Nov. 10, 2016)
2118	Le et al., Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade, Science 357:409–413 (July 28, 2017)
2119	Ethical Guidelines, Ethics in Clinical Research, NIH Clinical Center, https://www.cc.nih.gov/recruit/ethics (last accessed Sept. 26, 2024)
2120	The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research (April 18, 1979)

Exhibit Number	Description
2121	The Cancer Letter, Vol. 43, No. 38, Oct. 13, 2017
2122	The Cancer Letter, Vol. 48, No. 23, June 10, 2022
2123	How Beth Carner went from six weeks left to live with stage 4 colon cancer to complete remission, Cancer History Project (June 10, 2022), https://cancerhistoryproject.com/article/how-beth-carner-went-from-six-weeks-left-to-live-with-stage-4-colon-cancer-to-complete-remission/
2124	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (May 23, 2017)
2125	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (Oct. 2015)
2126	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (Aug. 2016)
2127	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (Mar. 2017)
2128	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (May 18, 2017)
2129	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (June 2020)
2130	Declaration of Dung Le, M.D.
2131	Investigator Initiated Clinical Trial Research Agreement between The Johns Hopkins University and Merck Sharp & Dohme Corp., dated August 14, 2013
2132	O'Neil et al, Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with advanced colorectal carcinoma, PLoS One (Dec. 28, 2017)
2133	FDA Grants Priority Review to Merck's Supplemental Biologics License Application (sBLA) Seeking Approval for KEYTRUDA® (pembrolizumab) for NewIndication in Microsatellite Instability-High Cancer. merck.com/news/fda-grants-priority-review-to-mercks-supplemental-biologics-license-application-sbla-seeking-approval-for-keytruda-pemb…
2134	News Release, Merck Makes $3 Million Charitable Donation to Support Swim Across America, Merck (Oct. 10, 2017), https://www.merck.com/news/merck-makes-3-million-charitable-donation-to-support-swim-across-america/

Exhibit Number	Description
2135	ASCO 2015: Mismatch Repair Deficiency Predicts Response to Pembrolizumab Among Patients With Colorectal and Other Cancers, The ASCO Post (May 29, 2015), https://ascopost.com/News/27670
2136	Video interview, Dung T. Le, MD, and Axel Grothey, MD, on PD-1 Blockade in Tumors With Mismatch Repair Deficiency, 2015 ASCO Annual Meeting, recorded on May 31, 2015, https://ascopost.com/archive/meetings/2015-asco-annual-meeting/dung-t-le-md-and-axel-grothey-md-on-pd-1-blockade-in-tumors-with-mismatch-repair-deficiency/
2137	Declaration of Ms. Jennifer Newberger
2138	K. Dickersin, Report from the panel on the Case for Registers of Clinical Trials at the Eighth Annual Meeting of the Society for Clinical Trials, Controlled Clinical Trials 9:76-81 (1988)
2139	D. Moher, Clinical-trial registration: a call for its implementation in Canada, CMAJ 149(11):1657-58 (Dec. 1, 1993)
2140	International Clinical Trials Registry Platform (ICTRP), World Health Organization, https://www.who.int/clinical-trials-registry-platform (last accessed Oct. 3. 2024)
2141	The Food and Drug Administration Modernization Act of 1997, Pub. L. 105–115, Nov. 21, 1997
2142	Laine et al., Update on Trials Registration: Clinical Trial Registration: Looking Back and Moving Ahead, ICMJE (June 2007)
2143	Food and Drug Administration Amendments Act of 2007, Pub. L. 110–85, Sept. 27, 2007, 121 Stat. 823
2144	RESERVED
2145	About ClinicalTrials.gov, Nat'l Library of Medicine, ClinicalTrials.gov, https://clinicaltrials.gov/about-site/about-ctg
2146	Krleza-Jerić et al., 7th Revision of the Declaration of Helsinki: Good News for the Transparency of Clinical Trials, Croat. Med. J. 50:105-10 (2009)
2147	42 C.F.R. Pt. 11 (2024)
2148	42 U.S.C. § 282(j)
2149	Protocol Registration Data Element Definitions for Interventional and Observational Studies, Nat'l Library of Medicine, ClinicalTrials.gov, https://clinicaltrials.gov/policy/protocol-definitions
2150	21 U.S.C. § 331 - Prohibited acts
2151	21 U.S.C. § 333 - Penalties

Exhibit Number	Description
2152	De Angelis et al., Clinical trial registration: a statement from the International Committee of Medical Journal Editors, Editorial, Clinical Trial Registration (2004)
2153	Response, The American Heritage dictionary of the English Language (5th ed. 2011)
2154	Response, Collins Dictionary (10th ed. 2009)
2155	Response, Oxford Dictionary of English, (3rd ed. 2010)
2156	Response, The Chambers Dictionary (13th ed. 2016)
2157	Response, Merriam-Webster's Collegiate Dictionary (11th ed. 2014)
2158	Response, Cambridge Advanced Learner's Dictionary (4th ed. 2013)
2159	Response, Webster's Third New International Dictionary of the English Language (2002)
2160	Plaintiff Merck Sharp & Dohme LLC's Opening Brief Regarding Claim Construction, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR, D.I. 82 (D. Md. May 1, 2024)
2161	The Johns Hopkins University's Opening Claim Construction Brief, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR, D.I. 81 (D. Md. May 1, 2024)
2162	Plaintiff Merck Sharp & Dohme LLC's Responsive Brief Regarding Claim Construction, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR, D.I. 107 (D. Md. May 1, 2024)
2163	Stenographic Deposition of Alfred I. Neugut, M.D., Ph.D., MPH taken on August 8, 2024, Merck Sharp & Dohme LLC, v. The Johns Hopkins University, Case IPR2024-00240 (PTAB)
2164	EX1096 from '187 proceeding, IPR2024-00649, Ajani et al., National Comprehensive Cancer Network. Gastric cancer, version 2.2013: featured updates to the NCCN Guidelines, J. Natl Compr. Canc. Netw., 11(5):531-46 (May 1, 2013)
2165	Record History Tab, Study of MK03475 in Patients with Microsatellite Unstable (MSI) Tumors (Cohorts A, B, and C), National Library of Medicine, ClinicalTrials.gov (Jan. 4, 2016), https://clinicaltrials.gov/study/NCT01876511?tab=history&a=12#version-content-panel
2166	Record History Tab, Study of MK03475 in Patients with Microsatellite Unstable (MSI) Tumors (Cohorts A, B, and C),

Exhibit Number	Description
	National Library of Medicine, ClinicalTrials.gov, Compare between June 10, 2013 and Jan. 4, 2016, https://clinicaltrials.gov/study/NCT01876511?tab=history&a=1&b=12#version-content-panel
2167	Highly Confidential Attorney Eyes Only Document 1 – Protective Order Material
2168	Highly Confidential Attorney Eyes Only Document 2 – Protective Order Material
2169	Highly Confidential Attorney Eyes Only Document 4 – Protective Order Material
2170	Highly Confidential Attorney Eyes Only Document 5 – Protective Order Material
2171	Highly Confidential Attorney Eyes Only Document 6 – Protective Order Material
2172	Highly Confidential Attorney Eyes Only Document 7 – Protective Order Material
2173	Highly Confidential Attorney Eyes Only Document 8 – Protective Order Material
2174	Highly Confidential Attorney Eyes Only Document 9 – Protective Order Material
2175	André et al., KEYNOTE-177 Investigators. Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer, N. Engl. J. Med., 383(23):2207-2218 (Dec. 3, 2023)
2176	Robin Marantz Henig, Could Immunotherapy Lead the Way to Fighting Cancer?, Smithsonian Magazine (April 2018), https://www.smithsonianmag.com/innovation/immunotherapy-lead-way-fighting-cancer-180968392/
2177	Exhibit 6, The Johns Hopkins University's Infringement of U.S. Patent No. 11,643,462 by KEYTRUDA claim chart, Merck Sharp & Dohme LLC v. The Johns Hopkins University, Case No. 1-22-cv-03059-JRR
2178	Marques et al., Tumor mutational burden in colorectal cancer: Implications for treatment, Crit. Rev. Oncol. Hematol. (Apr. 12, 2024)
2179	Le et al., Phase II Open-label study of pembrolizumab in treatment-refractory, microsatellite instability-high/mismatch repair-deficient

Exhibit Number	Description
	metastatic colorectal cancer: Keynote-164, J. Clin. Oncol. (38:1(1-19) (2019)
2180	Anagha Nair, High Impact Journals 2024 – Key to deciding the right journal?, Enago Academy (Feb. 19, 2024), https://www.enago.com/academy/top-high-impact-factor-journals/
2181	Highly Confidential Attorney Eyes Only Document 3 – Protective Order Material
2182	Highly Confidential Attorney Eyes Only Document 10 – Protective Order Material
2183	Email correspondence from Luis Diaz to Amy Meister and Mr. Robert Iannone dated December 27, 2012, production document Bates stamped JHU_MERCK00027065
2184	Breakthroughs in Immunotherapy, Swim Across America, https://www.swimacrossamerica.org/site/SPageNavigator/Breakthroughs_35.html (last accessed Sept. 26, 2024)
2185	RESERVED
2186	Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics, U.S. Dept. of HHS, FDA (May 2014)
2187-2188	RESERVED
2189	Email correspondence from Preston K. Ratliff to Nicholas Stephens and Casey Kraning dated August 20, 2024
2190-2204	RESERVED
2205	Accelerated Approval Letter to Nahid Latif of Merck Sharp and Dohme, Corp. from Patricia Keegan of the Department of Health and Human Services dated May 23, 2017 (https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/125514Orig1s014ltr.pdf)
2206-2250	RESERVED
2251	Siegel et al., Cancer Statistics, 2015, CA Cancer J. Clin., 65(1):5-29 (Jan-Feb 2017)
2252	Noone et al. (eds). SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2015/, based on November 2017 SEER data submission, posted to the SEER web site, April 2018

Exhibit Number	Description
2253	Canadian Cancer Society, Survival statistics for small intestine cancer, https://cancer.ca/en/cancer-information/cancer-types/small-intestine/prognosis-and-survival/survival-statistics
2254	American Cancer Society, Survival rates for bile duct cancer, https://www.cancer.org/cancer/types/bile-duct-cancer/detection-diagnosis-staging/survival-by-stage.html
2255	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Gastric Cancer, Version 4.2024 (August 12, 2024)
2256	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Pancreatic Adenocarcinoma, Version 3.2024 (August 2, 2024)
2257	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Hepatocellular Carcinoma
2258	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Biliary Tract Cancers
2259	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Small Bowel Adenocarcinoma, Version 1.2025 (December 4, 2024)
2260	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Ampullary Adenocarcinoma, Version 2.2024 (August 2, 2024)
2261	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Anal Carcinoma
2262	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Prostate Cancer, Version 1.2025 (December 4, 2024)
2263	RESERVED
2264	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Uterine Neoplasms, Version 3.2024 (September 20, 2024)
2265	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Ovarian Cancer, Version 3.2024 (July 15, 2024)

Exhibit Number	Description
2266	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Cervical Cancer, Version 4.2024 (September 24, 2024)
2267	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Neuroendocrine and Adrenal Tumors
2268	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Thyroid Carcinoma
2269	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer, Version 6.2024 (November 11, 2024)
2270	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Esophageal and Esophagogastric Junction Cancers, Version 4.2024 (July 30, 2024)
2271	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Testicular Cancer, Version 2.2024 (October 29, 2024)
2272	National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Head and Neck Cancers, Version 1.2025 (November 26, 2024)
2273	Highly Confidential Attorney Eyes Only – Protective Order Material: May 9, 2013 Submission
2274	Highly Confidential Attorney Eyes Only – Protective Order Material: June 11, 2013 Submission
2275	Highly Confidential Attorney Eyes Only – Protective Order Material: July 15, 2013 Submission
2276	Boland. Henry T. Lynch, MD (January 4, 1928–June 2, 2019), Gastroenterol., 157(4):905-906
2277	Aaltonen et al., Replication errors in benign and malignant tumors from hereditary nonpolyposis colorectal cancer patients, Cancer Res., 54:1645–1648 (1994)
2278	Aarnio et al., Cancer risk in mutation carriers of DNA-mismatch repair genes, Int. J. Cancer 81:214–218 (1999)
2279	Chen et al., Small bowel adenocarcinoma, Clin. Colon Rectal. Surg. 31:267-277 (2018)
2280	Center for Drug Evaluation and Research: Manual of Policies and Procedures, Office of New Drugs, “Review Designation Policy:

Exhibit Number	Description
	Priority (P) and Standard (S)," https://www.fda.gov/media/72723/download
2281	Hsiehchen et al., Mutation burden and anti-PD-1 outtcomes are not universally associated with immune cell infiltration or lymphoid activation, Cancer Cell 42:1985-1987 (2024)
2282	Stenographic Deposition of Alfred I. Neugut, M.D., Ph.D., MPH taken on January 6, 2025
2283-2299	RESERVED
2300	Merck & Co., Inc. KEYTRUDA® (pembrolizumab), Full Prescribing Information (March 2022)
2301	U.S. Patent No. 11,591,393
2302	Excerpts from Prosecution History of U.S. Patent No. 11,591,393
2303	Bonneville et al., Landscape of Microsatellite Instability Across 39 Cancer Types, American Society of Clinical Oncology ascopubs.org May 14, 2024
2304	Akagi et al. Real-world data on microsatellite instability status in various unresectable or metastatic solid tumors, Cancer Science (2021)
2305	FDA Approves Merck's Keytruda® Pembrolizumab for Patients With MSI-H/dMMR Advanced Endometrial Carcinoma, Who Have Disease Progression Following Prior Systemic Therapy in Any Setting and Are Not Candidates for Curative Surgery or Radiation (March 21, 2022)
2306-2400	RESERVED
2401	Copy of EX1001, U.S. Pat. No. 10,934,356, marked at January 6th Deposition of Dr. Neugut
2402	Copy of EX1005, ClinicalTrials.gov, NCT01876511, "Study of MK-3475 in Patients With Microsatellite Unstable (MSI) Tumors (Cohorts A, B and C)," (June 10, 2013), marked at January 6th Deposition of Dr. Neugut
2403	Board Email regarding Motion to Seal dated October 4, 2024
2404-2499	RESERVED
2500	Declaration of Frank E. Scherkenbach in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney

Exhibit Number	Description
2501	Declaration of Corrin N. Drakulich in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney
2502	Declaration of Christina D. Brown-Marshall in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney
2503	Declaration of Casey M. Kraning in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney
2504	Declaration of Madelyn S. McCormick in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney
2505	Declaration of Sarah E. Jack in Support of Notice of Intent to Designate a Provisionally Recognized PTAB Attorney
2506	Declaration of Caroline (Gracie) Koonce

Pursuant to 37 C.F.R. § 42.10(c), Patent Owner, The Johns Hopkins University ("Patent Owner" or "JHU") respectfully requests that the Board recognize Caroline (Gracie) Koonce as counsel *pro hac vice* in this proceeding. Patent Owner seeks the counsel of Ms. Koonce due to her experience in representing JHU in other patent-related matters and particularly due to her familiarity with the substantive and technical issues involved in this proceeding. This motion is authorized by the Notice of Filing Date Accorded to Petition and Time for Filing Patent Owner Preliminary Response that was mailed on April 12, 2024.

Petitioner does not oppose this motion.

Statement of Facts

Ms. Koonce is a patent litigation attorney with 2 years of experience representing clients in cases involving, *inter alia*, biochemistry and a variety of chemical and pharmaceutical innovations. Ms. Koonce regularly litigates patent cases before federal district courts and through her practice in such cases, Ms. Koonce has gained substantial experience in the various phases of patent litigation. Ms. Koonce's biography is attached as Appendix A of Exhibit 2506.

Ms. Koonce also has particular experience and familiarity with the substantive and technical issues involved in this inter partes review proceeding. In a related matter, Merck Sharp & Dohme LLC v. The Johns Hopkins University,

Case No. 1:22-CV-03059-JRR at the United States District Court for the District of Maryland, Ms. Koonce served as counsel for and specifically handled the patent-at-issue in this proceeding.

Declaration of Individual Seeking to Appear

This Motion for *Pro Hac Vice* Admission is accompanied by a Declaration of Caroline (Gracie) Koonce.

Accordingly, JHU submits that there is good cause under 37 C.F.R. § 42.10(c) for the Board to recognize Caroline (Gracie) Koonce as counsel *pro hac vice* during this proceeding.

Respectfully submitted,

Date: 03/18/2025

/Nicholas W. Stephens/

Nicholas Stephens, Reg. No. 74,320
Fish & Richardson P.C.
60 South Sixth Street, Suite 3200
Minneapolis, MN 55402

Attorney for Patent Owner

CERTIFICATE OF SERVICE

Pursuant to 37 CFR § 42.6(e)(4), the undersigned certifies that on March 18, 2025, a complete and entire copy of this Patent Owner's Motion for Pro Hac Vice and Exhibit 2506 were provided via email, to the Petitioner by serving the email correspondence addresses of record as follows:

Naveen Modi (Reg. No. 46,224)
Bruce M. Wexler (Reg. No. 35,409)
Preston K. Ratliff II (Reg. No. 43,034)
Daniel Zeilberger (Reg. No. 65,349)
David J. Feigenbaum (Reg. No. 78,139)
Mark Stewart (Reg. No. 43,936)
Paul Hastings LLP

PH-MSD-JHU-IPR@paulhastings.com
mark.stewart@merck.com

/Anastasia Renard/
Anastasia Renard
Fish & Richardson P.C.
60 South Sixth Street, Suite 3200
Minneapolis, MN 55402
renard@fr.com