

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MILTENYI BIOMEDICINE GmbH and MILTENYI BIOTEC INC.
Petitioners,

v.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA
Patent Owner.

IPR 2022-00852
Patent 9,518,123

IPR 2022-00855
Patent 9,540,445

PATENT OWNER'S EXHIBIT LIST

| Ex. | Reference |
|------|--|
| 2001 | Jason Fagone, <i>Has Carl June Found a Key to Fighting Cancer?</i> , PHILA. MAG. (Aug. 1, 2013). |
| 2002 | Denise Grady, <i>An Immune System Trained to Kill Cancer</i> , N.Y. TIMES (Sept. 12, 2011), https://www.nytimes.com/2011/09/13/health/13gene.html . |
| 2003 | Jasone Fagone, <i>Walt Keller, Leukemia Survivor, Has Passed</i> , PHILA. MAG. (Feb. 20, 2014), https://www.phillymag.com/news/2014/02/20/walt-keller-leukemia-survivor-obituary-1953-2014/ . |
| 2004 | Gina Kolata, <i>A Cancer Treatment Makes Leukemia Vanish, but Creates More Mysteries</i> , N.Y. TIMES (Feb. 2, 2022), https://www.nytimes.com/2022/02/02/health/leukemia-car-t-immunotherapy.html . |
| 2005 | Denise Grady, <i>In Girl's Last Hope, Altered Immune Cells Beat Leukemia</i> , N.Y. TIMES (Dec. 9, 2012), https://www.nytimes.com/2012/12/10/health/a-breakthrough-against-leukemia-using-altered-t-cells.html . |
| 2006 | Denise Grady, <i>F.D.A. Approves First Gene-Altering Leukemia Treatment, Costing \$475,000</i> , N.Y. TIMES (Aug. 30, 2017), https://www.nytimes.com/2017/08/30/health/gene-therapy-cancer.html . |
| 2007 | FOOD AND DRUG ADMIN., FDA APPROVAL BRINGS FIRST GENE THERAPY TO THE UNITED STATES (Aug. 30, 2017), https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states . |
| 2008 | FOOD AND DRUG ADMIN., BREAKTHROUGH THERAPY (Jan. 4, 2018), https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy . |
| 2009 | FOOD AND DRUG ADMIN., PRIORITY REVIEW (Jan. 4, 2018), https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review . |

| | |
|------|---|
| 2010 | Barbara Savoldo et al., <i>CD28 costimulation improves expansion and persistence of chimeric antigen receptor-modified T cells in lymphoma patients</i> , 121 J. CLINICAL INVESTIGATION 1822 (2011). |
| 2011 | Brian G. Till et al., <i>Adoptive immunotherapy for indolent non-Hodgkin lymphoma and mantle cell lymphoma using genetically modified autologous CD20-specific T cells</i> , 112 BLOOD 2261 (2008). |
| 2012 | Renier J. Brentjens et al., <i>Safety and persistence of adoptively transferred autologous CD19-targeted T cells in patients with relapsed or chemotherapy refractory B-cell leukemias</i> , 118 BLOOD 4817 (2011). |
| 2013 | Renier Brentjens et al., <i>Treatment of chronic lymphocytic leukemia with genetically targeted autologous T cells: case report of an unforeseen adverse event in a phase I clinical trial</i> , 18 MOLECULAR THERAPY 666 (2010). |
| 2014 | Renier J. Brentjens et al., <i>A Phase I Trial for the Treatment of Chemo refractory Chronic Lymphocytic Leukemia with CD19-Targeted Autologous T Cells</i> , 16 MOLECULAR THERAPY S15 (2008). |
| 2015 | Jennifer Couzin-Frankel, <i>The dizzying journey to a new cancer arsenal</i> , 340 SCI. 1514 (2013). |
| 2016 | Jennifer Couzin-Frankel, <i>Breakthrough of the Year 2013: Cancer Immunotherapy</i> , 342 SCI. 1432 (2013). |
| 2017 | David L. Porter et al., <i>Chimeric Antigen Receptor Modified T Cells Directed Against CD 19 (CTL01 9 cells) Have Long-Term Persistence And Induce Durable Responses In Relapsed, Refractory CLL</i> , 122 BLOOD 4162 (2013). |
| 2018 | David L. Porter et al., <i>Randomized, Phase II Dose Optimization Study Of Chimeric Antigen Receptor Modified T Cells Directed Against CD 19 (CTL019) In Patients With Relapsed Refractory CLL</i> , 122 BLOOD 873 (2013). |
| 2019 | Stephan A. Grupp et al., <i>T Cells Engineered With A Chimeric Antigen Receptor (CAR) Targeting CD 19 (CTL01 9) Produce Significant In Vivo Proliferation, Complete Responses And Long-Term Persistence</i> |

| | |
|------|---|
| | <i>Without GVHD In Children And Adults With Relapsed, Refractory ALL</i> , 122 BLOOD 67 (2013). |
| 2020 | James N. Kochenderfer et al., <i>B-cell depletion and remissions of malignancy along with cytokine-associated toxicity in a clinical trial of anti-CD 19 chimeric-antigen-receptor transduced T cells</i> , 119 BLOOD 2709 (2012). |
| 2021 | <i>Carl June Named One of Time's 100 Most Influential People in the World</i> , PENN MEDICINE (Apr. 26, 2018), https://pathology.med.upenn.edu/news/carl-june-named-one-times-100-most-influential-people-world . |
| 2022 | Holly Auer, <i>Penn Medicine Immunotherapy Pioneer Carl June, MD, Awarded 2015 Paul Ehrlich and Ludwig Darmstaedter Prize</i> , PENN TODAY (Mar. 11, 2015), https://penntoday.upenn.edu/news/penn-medicine-immunotherapy-pioneer-carl-june-md-awarded-2015-paul-ehrlich-and-ludwig-darmstaed . |
| 2023 | Andrew Pollock, <i>Setting the Body's 'Serial Killers' Loose on Cancer</i> , N.Y. TIMES (Aug. 1, 2016), https://www.nytimes.com/2016/08/02/health/cancer-cell-therapy-immune-system.html . |
| 2024 | <i>2015 Watanabe Award Winner Carl H. June</i> , IND. CLINICAL AND TRANSLATIONAL SCIS. INST., https://indianactsi.org/awards/watanabe-award-winners/2015-watanabe-award-winner-carl-h-june/ (last visited July 12, 2022). |
| 2025 | <i>Agilent Presents Thought Leader Award to Drs. Carl H. June and Michael Milone</i> , AGILENT TECHS. INC. (Nov. 17, 2020), https://www.agilent.com/about/newsroom/presrel/2020/17nov-ca20030.html . |
| 2026 | Information Disclosure Statement Initialed by Examiner (Apr. 18, 2016), U.S. Patent Application No. 14,997,136. |
| 2027 | Information Disclosure Statement Initialed by Examiner (Apr. 18, 2016), U.S. Patent Application No. 14,997,136. |

| | |
|------|---|
| 2028 | World Intell. Prop. Org. Patent Application No. WO 02/077029 A2. |
| 2029 | <i>Pilot Study for Patients with Chemotherapy Resistant or Refractory CD19 Leukemia and Lymphoma (CART-19)</i> , CLINICALTRIALS.GOV (April 29, 2009), [http://web.archive.org/web/20090903002304/http://clinicaltrials.gov/ct2/show/NCT00891215]. |
| 2030 | Amendments to the Claims (Nov. 13, 2018), U.S. Patent Application No. 15,353,899. |
| 2031 | Steven A. Rosenberg et al., <i>Use of Tumor-Infiltrating Lymphocytes and Interleukin-2 in the Immunotherapy of Patients with Metastatic Melanoma</i> , 319 NEW ENG. J. MED. 1676 (1988). |
| 2032 | Michael C. Jensen et al., <i>Antitransgene Rejection Responses Contribute to Attenuated Persistence of Adoptively Transferred CD20/CD19-Specific Chimeric Antigen Receptor Redirected T Cells in Humans</i> , 16 BIOLOGY BLOOD AND MARROW TRANSPLANTATION 1245 (2010). |
| 2033 | Richard A. Morgan et al., <i>Case Report of a Serious Adverse Event Following the Administration of T Cells Transduced With a Chimeric Antigen Receptor Recognizing ERBB2</i> , 18 MOLECULAR THERAPY 843 (2010). |
| 2034 | David L. Porter et al., <i>A phase I trial of donor lymphocyte infusions expanded and activated ex vivo via CD3/CD28 costimulation</i> , 107 BLOOD 1325 (2006). |
| 2035 | Grazyna Lipowska-Bhalla, <i>Targeted immunotherapy of cancer with CAR T cells: achievements and challenges</i> , 61 CANCER IMMUNOLOGY, IMMUNOTHERAPY 953 (2012). |
| 2036 | <i>Latest paper from the father of CAR-T: CAR-T really completely cured cancer</i> , MEDICALTREND.ORG, https://medicaltrend.org/2022/02/03/latest-paper-from-the-father-of-car-t-car-t-really-completely-cured-cancer/ (last visited July 13, 2022). |
| 2037 | Bipulendu Jena et al., <i>Redirecting T-cell specificity by introducing a tumor-specific chimeric antigen receptor</i> , 116 BLOOD 1035 (2010). |

| | |
|------|--|
| 2038 | Michael H. Kershaw et al., <i>A Phase I Study on Adoptive Immunotherapy Using Gene-Modified T Cells for Ovarian Cancer</i> , 12 CLINICAL CANCER RSCH. 6106 (2006). |
| 2039 | Cor H.J. Lamers et al., <i>Treatment of Metastatic Renal Cell Carcinoma With Autologous T-Lymphocytes Genetically Retargeted Against Carbonic Anhydrase IX: First Clinical Experience</i> , 24 J. CLINICAL ONCOLOGY e20 (2006). |
| 2040 | <i>ASH honors Bruce R. Blazar, M.D., and Carl H. June, M.D., with 2012 Ernest Beutler Lecture and Prize</i> , SCIENCE X (Aug. 27, 2012), https://sciencex.com/wire-news/107531358/ash-honors-bruce-r-blazar-md-and-carl-h-june-md-with-2012-ernest.html . |
| 2041 | Renier J. Brentjens et al., <i>Genetically Targeted T Cells Eradicate Systemic Acute Lymphoblastic Leukemia Xenografts</i> , 13 CLINICAL CANCER RSCH. 5426 (2007). |
| 2042 | U.S. Patent No. 7,402,431. |
| 2043 | <i>Cancer treatment myths: Any truth to these common beliefs?</i> , MAYO CLINIC (March 22, 2022), https://www.mayoclinic.org/diseases-conditions/cancer/in-depth/cancer/art-20046762 . |
| 2044 | Adam Bagg Aff., July 19, 2022. |
| 2045 | <i>SITC Smalley Award 2013 Recipient</i> , SOC’Y FOR IMMUNOTHERAPY OF CANCER, https://www.sitcancer.org/funding/named-funds-and-awards2/smalley/2013 (last visited July 19, 2022). |
| 2046 | <i>AAI-Steinman Award for Human Immunology Research Past Recipients</i> , AM. ASS’N OF IMMUNOLOGISTS, https://www.aai.org/Awards/Career-Awards/AAI-Steinman-Award-for-Human-Immunology-Research/Past-Recipients.aspx (last visited July 19, 2022). |
| 2047 | File History of the ’445 Patent. |
| 2048 | Decl. of Thomas S. Fletcher, Nov. 8, 2022. |

| | |
|------|--|
| 2049 | <i>Search Results of Clinical Trials Associated with Dr. Richard P. Junghans</i> , CLINICALTRIALS.GOV (Jan. 12, 2023), https://beta.clinicaltrials.gov/search?distance=SO&term=Richard Junghans . |
| 2050 | <i>Recombinant DNA Advisory Committee Minutes of Meeting</i> , US DEP'T OF HEALTH & HUM. SERVS., (Feb. 10, 2003). |
| 2051 | <i>Recombinant DNA Advisory Committee Minutes of Meeting</i> , US DEP'T OF HEALTH & HUM. SERVS., (Mar. 16, 2005). |
| 2052 | Hildegund C.J. Ertl et al., <i>Considerations for the Clinical Application of Chimeric Antigen Receptor (CAR) T Cells: Observations from a Recombinant DNA Advisory Committee (RAC) Symposium June 15, 2010</i> , 71 CANCER RES. 1 (2011). |
| 2053 | Augusto C. Ochoa et al., <i>Immune Defects in T Cells From Cancer Patients: Parallels in Infectious Diseases</i> , in CURRENT CLINICAL ONCOLOGY: CANCER IMMUNOTHERAPY AT THE CROSSROADS: HOW TUMORS EVADE IMMUNITY AND WHAT CAN BE DONE 35 (J. H. Finke & R. M. Bukowski eds., 2004). |
| 2054 | Peter S. Kim et al., <i>Features of responding T cells in cancer and chronic infection</i> , 22 CURRENT OPINION IN IMMUNOLOGY 223 (2010). |
| 2055 | Marta Czesnikiewicz-Guzik et al., <i>T cell subset-specific susceptibility to aging</i> , 127 CLINICAL IMMUNOLOGY 107 (2008). |
| 2056 | Jonathan E. Benjamin et al., <i>Biology and clinical effects of natural killer cells in allogeneic transplantation</i> , 22 CURRENT OPINION IN ONCOLOGY 130 (2010). |
| 2057 | Elisabeth Ersvaer et al., <i>Intensive chemotherapy for acute myeloid leukemia differentially affects circulating T_{C1}, T_{H1}, T_{H17} and T_{REG} cells</i> , 11 BMC IMMUNOLOGY 1 (2010). |
| 2058 | Mirosław J. Szczepanski, <i>Increased Frequency and Suppression by Regulatory T Cells in Patients with Acute Myelogenous Leukemia</i> , 15 CLINICAL CANCER RSCH. 3325 (2009). |
| 2059 | Sabine Mumprecht et al., <i>Programmed death 1 signaling on chronic myeloid leukemia-specific T cells results in T-cell exhaustion and disease progression</i> , 114 BLOOD 1528 (2009). |
| 2060 | Gideon Gross et al., <i>Expression of immunoglobulin-T-cell receptor chimeric molecules as functional receptors with antibody-type specificity</i> , 86 IMMUNOLOGY 10024 (1989). |

| | |
|------|---|
| 2061 | Anna Kruschinski et al., <i>Engineering antigen-specific primary human NK cells against HER-2 positive carcinomas</i> , 105 PROC. OF THE NAT'L ACAD. OF THE SCIS. 17481 (2008). |
| 2062 | Olan Dolezal et al., <i>ScFv multimers of the anti-neuraminidase antibody NC10: shortening of the linker in single-chain Fv fragment assembled in V_L to V_H orientation drives the formation of dimers, trimers, tetramers and higher molecular mass multimers</i> , 13 PROTEIN ENG'G 565 (2000). |
| 2063 | Michael C. Milone et al., <i>Chimeric Receptor Containing CD137 Signal Transduction Domains Mediate Enhanced Survival of T Cells and Increased Antileukemic Efficacy In Vivo: Supplementary Materials and Methods</i> , 17 MOLECULAR THERAPY 1453 (2009). |
| 2064 | T. Sutlu et al., <i>Natural killer cell-based immunotherapy in cancer: current insights and future prospects</i> , 266 J. INTERNAL MED. 154 (2009). |
| 2065 | Chihaya Imai et al., <i>Genetic modification of primary natural killer cells overcomes inhibitory signals and induces specific killing of leukemic cells</i> , 106 BLOOD 376 (2005). |
| 2066 | Curriculum Vitae of Robert S. Negrin, M.D. (Feb. 10, 2023). |
| 2067 | Hollie J. Pegram et al., <i>Adoptive Transfer of Gene-Modified Primary NK Cells Can Specifically Inhibit Tumor Progression In Vivo</i> , 181 THE J. IMMUNOLOGY 3449 (2008). |
| 2068 | Loredana Ruggeri et al., <i>Effectiveness of donor natural killer cell alloreactivity in mismatched hematopoietic transplants</i> , 295 SCI. 2097 (2002). |
| 2069 | Güllü Görgün et al., <i>Chronic lymphocytic leukemia cells induce changes in gene expression of CD4 and CD8 T cells</i> , 115 J. CLINICAL INVESTIGATION 1797 (2005). |
| 2070 | Transcript of Deposition of Richard P. Junghans, Ph.D., M.D. (Jan. 13, 2023). |
| 2071 | Declaration of Robert S. Negrin, M.D. (Feb. 13, 2023). |
| 2072 | John Carroll, <i>Novartis may still be grappling with Kymriah sales, but historic CAR-T promise still shines through 5-year data</i> , ENDPOINTSNEWS (June 13, 2022), https://endpts.com/novartis-may-still-be-grappling-with-kymriah-sales-but-historic-car-t-promise-still-shines-through-5-year-data/ . |

| | |
|------|---|
| 2073 | Veronique Blanc et al., <i>SAR3419: An Anti-CD19-Maytansinoid Immunoconjugate for the Treatment of B-Cell Malignancies</i> , 17 CLINICAL CANCER RSCH. 6448 (2011). |
| 2074 | Robert T. Abraham et al., <i>Jurkat T cells and development of the T-cell receptor signalling paradigm</i> , 4 NATURE REV. IMMUNOLOGY 301 (2004). |
| 2075 | Rebekah R. Bartelt et al., <i>Comparison of T Cell Receptor-Induced Proximal Signaling and Downstream Functions in Immortalized and Primary T Cells</i> , 4 PLOS ONE 1 (2009). |
| 2076 | Zhaosheng Lin et al., <i>Comparative Microarray Analysis of Gene Expression During Activation of Human Peripheral Blood T Cells and Leukemic Jurkat T Cells</i> , 83 LAB’Y INVESTIGATION 765 (2003). |
| 2077 | Louis Gioia et al., <i>A genome-wide survey of mutations in the Jurkat cell line</i> , 19 BMC GENOMICS 1 (2018). |
| 2078 | Michael C. Milone et al., <i>Corrigendum to “Chimeric Receptors Containing CD137 Signal Transduction Domains Mediate Enhanced Survival of T Cells and Increased Antileukemic Efficacy In Vivo,”</i> 23 MOLECULAR THERAPY 1278 (2015). |
| 2079 | <i>Kymriah®: Highlights of Prescribing Information</i> , NOVARTIS PHARMS. CORP. (May 2022). |
| 2080 | Jacqueline Corrigan-Curay et al., <i>T-Cell Immunotherapy: Looking Forward</i> , 22 MOLECULAR THERAPY 1564 (2014). |
| 2081 | Steven C. Katz et al., <i>Phase I Hepatic Immunotherapy for Metastases study of intra-arterial chimeric antigen receptor modified T cell therapy for CEA+ liver metastases</i> , 21 CLINICAL CANCER RSCH. 1 (2015). |

Certification of Service Under 37 C.F.R. § 42.6(e)(4)

The undersigned hereby certifies that Patent Owner's Exhibit List was served in its entirety by filing through the Patent Trial and Appeal Case Tracking System (P-TACTS), as well as providing a courtesy copy via e-mail to the following attorneys of record for Petitioners listed below:

| | |
|--------------------|---------------------------|
| Yite John Lu | PTABDocketL2Y7@orrick.com |
| Gary N. Frischling | PTABDocketG2F1@orrick.com |

Date: February 13, 2023

By: /Jessamyn S. Berniker/

Reg. No. 72,328