U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
168th NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
4 September 2024

Conference Room TE406, East Wing, Shady Grove Campus
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
4 September 2024

The National Cancer Advisory Board (NCAB) convened for its 168th regular meeting on 4 September 2024. The meeting was open to the public on Wednesday, 4 September 2024, from 9:00 a.m. to 3:15 p.m. and closed to the public from 3:35 p.m. to 4:10 p.m. The NCAB Chair, Dr. John D. Carpten, Director, Comprehensive Cancer Center, Director and Chief Science Officer, Beckman Research Institute of City of Hope, presided during both the open and closed sessions.

NCAB Members

Dr. John D. Carpten (Chair)
Ms. Margaret Anne Anderson
Dr. Nilofer S. Azad
Dr. Anna D. Barker
Dr. Richard J. Boxer
Dr. Callisia N. Clarke*
Dr. Luis Alberto Diaz, Jr.
Dr. Andrea Hayes Dixon
Ms. Ysabel Duron (absent)
Dr. Karen M. Emmons*
Ms. Tamika Felder*
Dr. Howard J. Fingert (absent)
Dr. Christopher R. Friese
Ms. Julie Papanek Grant
Dr. Amy B. Heimberger
Dr. Nikan Khatibi (absent)
Dr. Ana Navas-Acien (absent)
Dr. Edjah K. Nduom*
Dr. Fred K. Tabung
Dr. Susan Thomas Vadaparampil
Dr. Ashani T. Weeraratna
Dr. Karen M. Winkfield

* Pending appointment

President's Cancer Panel

Dr. Elizabeth M. Jaffee (Chair) (absent)
Dr. Mitchel S. Berger (absent)
Dr. Carol L. Brown (absent)

Alternate *Ex Officio* NCAB Members

Dr. John Gordon, CPSC
Dr. Joseph R. Graber, DOE (absent)
Dr. Michelle L. Heacock, NIEHS
Dr. Michael Kelley, VA (absent)
Dr. Richard Pazdur, FDA (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. W. Kimryn Rathmell, Director, National Cancer Institute
Dr. Jill S. Barnholtz-Sloan, Acting Director, Center for Biomedical Informatics and Information Technology
Dr. Oliver Bogler, Director, Center for Cancer Training
Dr. Philip E. Castle, Director, Division of Cancer Prevention
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. James H. Doroshow, Director, Division of Cancer Treatment and Diagnosis
Dr. Dan Gallahan, Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Center for External Affairs
Dr. Katrina A.B. Goddard, Director, Division of Cancer Control and Population Sciences
Dr. Satish Gopal, Director, Center for Global Health
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. James Gulley, Acting Co-Director and NCI Clinical Director, Center for Cancer Research
Dr. Ed Harlow, Special Advisor to the NCI Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Warren A. Kibbe, Deputy Director for Data Science and Strategy
Dr. Kristin Komschlies McConville, Acting Director, Office of Scientific Operations, NCI at Frederick
Ms. Amber Lowery, Executive Officer and Deputy Director for Management, Office of the Director
Dr. Douglas R. Lowy, Principal Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Acting Co-Director and Scientific Director for Basic Research, Center for Cancer Research
Dr. Meg Mooney, Associate Director, Cancer Therapy Evaluation Program
Dr. Diane Palmieri, Director, Center for Research Strategy
Dr. Krzysztof Ptak, Acting Director, Office of Cancer Centers
Dr. Henry Rodriguez, Director, Office of Cancer Clinical Proteomics Research
Mr. Jeffrey Shilling, Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Biomedical Informatics and Information Technology
Dr. Dinah S. Singer, Deputy Director, Scientific Strategy and Development
Dr. Sanya A. Springfield, Director, Center for Cancer Health Equity
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Dr. Carol J. Thiele, Interim Director, Center for Cancer Research
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
Dr. Brigitte C. Widemann, Special Advisor to the Director for Childhood Cancer
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Diane, Palmieri, Executive Secretary, Office of the Director

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WEDNESDAY, 4 SEPTEMBER 2024

I. CALL TO ORDER AND OPENING REMARKS—DR. JOHN D. CARPTEN

Dr. John D. Carpten called to order the 168th National Cancer Advisory Board (NCAB) meeting. He welcomed members of the Board, *ex officio* members, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Carpten reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to accept the minutes of the 11-22 June 2024 Joint Meeting of the Board of Scientific Advisors (BSA) and the NCAB was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. JOHN D. CARPTEN

Dr. Carpten called Board members' attention to the future meeting dates listed on the agenda.

III. NCI DIRECTOR'S REPORT—DR. W. KIMRYN RATHMELL

Dr. W. Kimryn Rathmell, Director, NCI, welcomed NCAB members and attendees to the 168th regular meeting and reported on recent news and updates, the budget, and research and program highlights.

NCI Recent News and Updates. Dr. Rathmell highlighted a summer of visits and meetings with both local and international NCI collaborators. She got better acquainted with the NCI Community Oncology Research Program (NCORP) and visited sites at (1) The University of Kansas, which has a federated system that provides insight on delivering care across a vast region of the Midwest, and (2) Bronx, New York, which has two Minority/Underserved Community Sites (MU-NCORP): Montefiore Medical Center, Einstein Campus, and Columbia University with a subaffiliate at the James J. Peters Department of Veterans Affairs Medical Center. The Montefiore Einstein site serves a smaller geography and offers services to patients who speak 27 languages. Its patient population is 32 percent immigrants, and 30 percent have poverty-level incomes. Remarkably, in this setting, the site has reported record clinical trial enrollment and was the first to participate in NCI's Virtual Clinical Trials Office Pilot Program, which focuses on streamlining the opening of clinical trials. Dr. Rathmell remarked that NCI can gain insight from these sites where patients receive their care and that these sites possess a talent pool of community oncologists.

Dr. Rathmell also visited NCI-sponsored programs that support training. The University of Colorado Anschutz Medical Campus Medical Scientist Training Program hosts the Annual M.D.-Ph.D. National Student Conference, and Dr. Rathmell was a keynote speaker at the 2024 conference, held in Breckenridge, Colorado. During that conference, Dr. Rathmell discussed with future physician-scientists why cancer research is the field that they should develop. In addition, she visited The University of Chicago Medicine's Comprehensive Cancer Center, which was celebrating its 50th anniversary and hosting its 10th Annual Summer Research Symposium, during which it highlighted its students from high school and undergraduate training. In addition, The University of Chicago Youth Enjoy Science (YES) program is a flagship NCI program that was recently approved by BSA for renewal. Other NCI training programs being piloted by the Center for Cancer Training (CCT) and the Center for Cancer Health Equity (CCHE) include partnering with community colleges, such as the Malcolm X College, on equipping associate degree students with the skills to be part of a clinical trials office at their respective institutions.

As part of building NCI's relationships globally, a World Health Organization (WHO) delegation visited NCI and the National Institutes of Health (NIH). An ongoing collaboration with NCI's Center for Global Health (CGH) and the WHO is the NCI WHO Collaborating Center for Global Cancer Control. NCI hosted the U.S. Ambassador to Australia, Ms. Caroline Kennedy, and discussed efforts toward human papillomavirus (HPV) vaccination and the eradication of cervical cancer. NCI also met with senators from Australia who were touring the United States. To address where larger-scale collaborations can happen across scientific interests, NCI hosted a coalition from the National Cancer Center in Japan, which was visiting NIH. Later in September, NCI will host a symposium on oncology at which Dr. Rathmell, Dr. Philip E. Castle, Director, Division of Cancer Prevention (DCP), and Dr. James Gulley, Acting Co-Director and NCI Clinical Director, Center for Cancer Research (CCR), will present keynote addresses. Dr. Satish Gopal, Director, CGH, attended the first U.S.–India dialogue, which was hosted in person in India and virtually. Additional areas of interest and opportunities for collaborating with other countries include immunology, artificial intelligence (AI), and technology. Australia, India, Japan, and the United States comprise the Quad forum of four countries that have committed to tackling the world's most complicated problems, one of which is cancer.

Dr. Rathmell reviewed the most recent White House engagements on cancer topics. NCI held discussions with Office of Management and Budget (OMB) examiners about the outcomes of the Cancer Moonshot℠ and those investments during their visit to NIH. The OMB examiners returned for a tour of the Frederick National Laboratory for Cancer Research (FNLCR) to learn more about its capabilities. NCI also has been working with the U.S. Department of Health and Human Services (HHS) Deputy Secretary, Ms. Andrea Palm, about meetings that piqued her interest regarding NCI's capabilities. NCI invited her to its campus which included a virtual visit of the FNLCR. During that visit, Ms. Palm and NCI discussed worldwide efforts where the cancer community can make a significant difference, including with HPV.

On 16 July 2024, NCI hosted its first Annual Scientific Priorities Retreat. Attendees included chairs of its seven Boards and members of the community. The goal was to survey the landscape of cancer initiatives to identify focus areas where NCI can demonstrate output and value to the public. The key themes included ways to build trust, demonstrate trustworthiness, engage communities, and communicate good science. Tangible outputs of the retreat will be announced at a future Board meeting.

Dr. Rathmell announced new leadership positions, appointed following national searches and review of internal candidates. She noted that Mr. Peter Garrett was selected as Director, Center for External Affairs (CEA). He previously led NCI's Office of Communications and Public Liaison (OCPL). The CEA will work closely with NCI's OCPL, Office of Government and Congressional Relations (OGCR), and Office of Advocacy Relations on engaging with communities, communicating effectively across this broad area, and bringing all resources together moving forward. Ms. Amber Lowery is now Deputy Director for Management and Executive Officer. She previously served as NCI's Acting Deputy Director for Management and Executive Officer. In addition, Dr. Warren A. Kibbe is the inaugural NCI Deputy for Data Science and Strategy. Dr. Rathmell encouraged visiting the Center for Biomedical Informatics and Information Technology (CBIIT) blog, *Cancer Data Science Pulse*, for further information about NCI's data science efforts.

NCI Budget. Dr. Rathmell focused her budget update on the NCI Professional Judgment Budget Proposal (also called the Bypass Budget). The Professional Judgment Budget estimates the cost of the work that NCI is expected to perform and is reported directly to Congress. The *Annual Plan and Budget Proposal for Fiscal Year (FY) 2026* was recently released and includes three cancer research stories: (1) Justin, an NCI innovative clinical trial participant with non-Hodgkin's lymphoma refractory to all conventional therapies, has been disease free for 3 years from his start on the trial; (2) early stage investigator (ESI) and Cancer Moonshot scholar, Dr. Leeya Pinder, is working on cervical cancer prevention and bringing this research to lower-resource areas; and (3) a company supported by NCI's

Small Business Innovation Research (SBIR) program is investigating a molecule that can detect cancer cells in the operative field. This SBIR story is showcasing how technology blends with science, innovation, and medicine and is a part of NCI's economic engine.

For the 2026 Professional Judgment Budget, NCI proposed a budget of $11.5 billion (B), which reflects an investment in cancer research that can capitalize on opportunities that have had high returns on investment (ROIs), including cancer prevention research, training and infrastructure, and discovery. NCI understands the financial reality that real economic constraints face our country and the world, but it wanted to illustrate the need for an infusion of appropriations to do the work that people are expecting NCI to do. At this rate, NCI risks losing its competitive edge, falling behind its peers, and losing a generation of workers. To prioritize the research, the 2026 Professional Judgment Budget focuses on four scientific opportunities: tackling the emergence of early-onset cancers in young adults; approaching cancer as a disease that affects the entire body; alleviating financial toxicity for cancer survivors and caregivers; and expanding the utility of cancer-targeting vaccines.

Dr. Rathmell noted that the 2023 Professional Judgment Budget proposal was $7.7B but that the enacted budget was $7.3B. For the 2024 Bypass, NCI proposed a budget increase to $9.9B but received $7.2B enacted. NCI was allotted an increase to enable its work, but the net decrease was $96 million (M). Inflation has been increasing more than the budget estimates for several years. For the FY 2025 Professional Judgment Budget proposal, NCI proposed $11B; the FY 2026 proposal remains at this level. NCI is committed to prioritizing and investing in training and ESIs and talent development. Since FY 2016, NCI has increased paylines for ESIs R01/R37 by 6 percent, resulting in an increase from the 12th to 17th percentile. NCI established paylines for FY 2024 at the 10th percentile for R01 grants to established and new investigators, 14th percentile for R01 grants to ESIs, and 10th percentile for R21 exploratory grants.

The National Cancer Plan (NCP) is a roadmap for defining the cancer agenda for the nation, with a key goal of making significant advancements in cancer, which affects how NCI allocates its budget. NCI is focusing on optimizing the workforce and has planned community engagement efforts from September 2024 to December 2024. Dr. Rathmell described several examples to support this effort. NCI is promoting the R15 grant program, which supports investigators at institutions without high levels of NIH funding. NCI is partnering with the American Cancer Society (ACS) to sponsor the Catalyst Awards and postdoctoral fellowship grants to help fund ESIs with their high-scoring, but unfunded, research projects. In addition, the President's Cancer Panel will host the "Developing and Retaining a Robust and Diverse Cancer Workforce: Challenges and Opportunities Across the National Cancer Program" two-part virtual open dialogue on the cancer workforce.

Cancer Research and Program Highlights. Dr. Rathmell reported on recent research advances in immunotherapy, RAS research, and population science. On 2 August 2024, U.S. Food and Drug Administration (FDA) approved the first T-cell receptor therapy for advanced synovial sarcoma. Since June 2024, FDA has approved three immunotherapies for endometrial cancer. As part of the Women's Health Initiative, NCI solicited supplements to increase its research portfolio in endometrial cancer projects and boost that pipeline of researchers. The RAS Initiative is investigating *RAS* genes; *KRAS*, one of three human *RAS* genes that previously were considered "undruggable" in their mutant, cancer-causing forms, is showing tremendous output. *RAS* genes are involved in cell growth, cell maturation, and cell death and are mutated in more than 30 percent of cancers. *KRAS* is one of three human *RAS* genes. The investigators have reported new information about the structure and function of the KRAS 4a variant and have discovered a first dual inhibitor of the KRAS for tumors with the G12C mutation, which is the most common mutation found in lung cancer. From the perspective of population health, the Division of Cancer Control and Population Sciences (DCCPS) investigators reported a new analysis showing the cost

of cancer screening, an estimated $43B in the United States, is less than the annual cost of treatment within the first 12 months after a diagnosis, suggesting that early screening is cost-effective.

In closing, Dr. Rathmell solicited the NCAB members to provide input on where the new CEA should focus in terms of communications; insights on how NCI is meeting the needs of the workforce, AI advances, community-based oncology research, and pediatric oncology; and how to best leverage existing resources or form new partnerships.

Questions and Answers

NCAB Chair Dr. Carpten asked about an analysis comparing U.S. investments in cancer research with other countries that have high gross domestic products, such as the United Kingdom or China, and whether they have a competitive advantage. Dr. Rathmell noted that the United States is the largest funder of cancer research worldwide, but she could not speak about how that factors on a per capita basis and how it compares to parts of the NCI budget.

Dr. Andrea Hayes Dixon, Dean, Howard University College of Medicine, Vice President of Clinical Affairs, Chair of Surgery, Howard University Hospital, asked about opportunities for improving communications with community partners during the summer visits and whether they felt connected to NCI. Dr. Rathmell noted conversations with community leaders in Kansas and New York who were seeking ways to connect with NCI. The challenge is to understand ways to penetrate the vast amount of existing information to have a reliable source of trustworthy information, which NCI prioritizes. NCI also is learning how best to reach people, especially busy community oncologists who work in remote, rural areas of the United States. The NCI-Designated Cancer Centers (Cancer Centers) play a significant role in making sure messages are not lost and can reach the people who need them.

Dr. Anna D. Barker, Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California, called attention to the American Association for Cancer Research (AACR) Scientist↔Survivor Program® that has been ongoing for the past 25 years. The AACR recently added educational programs for advocates to the Scientist↔Survivor Program as a virtual forum in which as many as 30 countries are participating. She emphasized that the advocacy movement is moving in an international direction and suggested focusing on building alliances with and influencing other countries in future efforts. Dr. Rathmell commented on having advocates engaged in discussions about NCI priorities during the Annual Scientific Priorities Retreat.

Ms. Margaret Anne Anderson, Managing Director, Deloitte Consulting LLP, asked about the study that found the cost of cancer screening is less than the total cost of treatment, and how these findings connect to NCI programs or different advocacy efforts. Patients with cancer are not availing themselves of early screening, nor are their physicians discussing it, resulting in higher treatment costs. Dr. Rathmell noted that the key message about early screening has gained attention in the news media, including *The New York Times.* NCI relies on DCCPS to convey these strong messages and the DCP to identify a study in which to put these findings into practice and into the public consciousness to better understand the questions people are asking, which is economically significant. It can be challenging for an individual to decide about the benefits of an expensive screening test relative to its affordability. The value lies in NCI's being able to communicate this critical message to the public.

Dr. Nilofer S. Azad, Professor of Oncology, Co-Director, Developmental Therapeutics Program, Co-Leader, Cancer Genetics and Epigenetics, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, commented that considering the amount of research being led by private industry, NCI has an opportunity to position itself to leverage industry dollars, especially because the NCI budget will not meet all the needs of cancer research. Partnering with large companies that have launched new screening technologies could free up NCI investments for supporting junior investigators. Issues

regarding for-profit versus nonprofit companies will need to be addressed and will require structural changes in the way that NCI conducts its business. Dr. Rathmell agreed that working together across all lines, including private industry, is necessary for advancing cancer research.

Dr. Susan Thomas Vadaparampil, Associate Center Director, Community Outreach, Engagement, and Equity, Professor, Department of Health Outcomes and Behavior, Moffitt Cancer Center, commented on the utility of findings and how they reverberate in the cancer community. Scientific studies covered by the local news and local policymakers have been one way that NCI has been promoting evidence that informs investments in screening, for example. This approach is a great tool for the Cancer Centers. NCAB Chair Dr. Carpten added that the breakdown of the programmatic funding for cancer control was less than funding for treatment and therapeutics. Discussions about shifting the balance should be considered.

Dr. Edjah K. Nduom, Daniel Louis Barro Endowed Chair, Associate Professor, Department of Neurosurgery, Emory University School of Medicine, Brain Tumor Disease Leader, Winship Cancer Institute, was impressed with the screening-versus-treatment and ROI information. He spoke on the importance of government's investing in science for rare cancers, which is limited in industry. Once those investments are made, industry benefits. He asked Dr. Rathmell about her thoughts on how to generate and present more data that address ROI, which may be different for ESIs and established investigators. Dr. Rathmell responded that the ROI for the public translates as healthy Americans, but the effect on the economy can be broken down differently. For example, having a talented, skilled workforce making discoveries that will affect cancer today and health tomorrow or other facets of biology is an important aspect. Equally important is stimulating the economy with new companies and de-risking cancer research, which is one asset of having FNLCR and various NCI programs.

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, pointed out that the Cancer Intervention and Surveillance Modeling Network (CISNET) and DCCPS investigators published a report illustrating the number of cancer patient lives that could be saved with a 10-percent increase in screening interventions across several cancer types. Dr. Lowy will forward this report to the NCAB members.

Ms. Julie Papanek Grant, General Partner, Canaan, asked whether ESIs were a priority in NCI's workforce development effort and whether other gaps in the national cancer workforce should be prioritized based on existing data. Dr. Rathmell noted that workforce development is a priority for NCI and involves all career stages, including sponsoring programs for high school and undergraduate students. She remarked that workforce development also extends to those who provide care to patients, such as nurse practitioners and community oncologists. NCI emphasizes ESIs and postdoctoral scholars because they are central to the field and what it needs, especially given that the average age for receiving a first R01 grant is in the late 40s. Overcoming this gap requires preparing these investigators and getting them into the funding pool earlier, which entails maintaining a strong cancer career pipeline. In the next 3 months of NCI communications, messages on optimizing the workforce will be broad. Ms. Grant emphasized that workforce development efforts should include jobs tied to the implementation of cancer care, such as nurses, clinical trial coordinators, and clinical trial managers.

Dr. Callisia N. Clarke, Chief, Division of Surgical Oncology, Associate Professor of Surgery, Department of Surgery, Medical College of Wisconsin, was pleased to see the efforts on developing and maintaining a workforce that is strong and diverse, which have been underrecognized and underfocused on for some time. Discussions of introducing innovative treatments for cancer should recognize that implementation of these treatments often widens the disparities in cancer outcomes for people without access to the treatments. This discordance in care has been seen racially, from a gender standpoint, and especially from a first-language perspective. These factors affect a patient's ability to either undergo cancer screening or receive cancer treatment. Until the cancer community focuses on making sure that the

workforce represents cancer patients, it will consistently chase cancer disparities. Dr. Clarke is excited to see that the President's Cancer Panel will discuss this topic and encourages the NCAB and NCI to understand why it is critical to recognize this as an important pillar of developing innovative treatments.

Dr. Fred K. Tabung, Assistant Professor, Department of Internal Medicine, College of Medicine and Comprehensive Cancer Center, The Ohio State University, commented on the compelling data on the benefits of screening versus treatment. He asked about plans for balancing clinical testing with the science, given the optimism on Capitol Hill. Dr. Rathmell noted that sometimes the science outpaces the clinical testing, and other times the clinical testing is ahead of the science. NCI's job is to design studies that provide the necessary information to make sound decisions.

IV. BUDGET UPDATE—MR. WESTON RICKS AND DR. DOUGLAS R. LOWY

Mr. Weston Ricks, Director, Office of Budget and Finance, NCI, reviewed the budget landscape for NCI activities over time. He expressed appreciation to NCI Office of Extramural Finance and Information Analysis staff, Ms. Tenille McCatty and Ms. Linli Liu, and Dr. Christine Burgess from the NCI Center for Research Strategy, for their assistance with updating the budget data for this presentation. Mr. Ricks explained that NCI's budget, which NCI leadership and stakeholders (community and research) consider, supports several initiatives, including the Specialized Programs of Research Excellence (SPORE), clinical cooperative groups, the NIH Clinical Center, and the SBIR/Small Business Technology Transfer programs. He emphasized that some programs or activities take more time than others to come to fruition.

Mr. Ricks summarized several aspects of research and operations that consume the NCI budget. One aspect is inflation. The Biomedical Research and Development Price Index (BRDPI), an inflationary price index associated with biomedical research, was established by and is managed by NIH. The BRDPI is released annually, and for NCI, it shows that in 2003, the buying power and the budget (normalized) were the same but became unsynchronized in 2013, when NCI's budget significantly decreased. Although NCI has had significant budget increases, it has not yet reached the parity of 2003. NCI has 15 percent less buying power in 2024 than it did in 2003. Another aspect is the competing needs (e.g., security, transportation, infrastructure) across the federal government, as well as the global requirements and decisions that confluence priorities. In FY 2023, NCI received a $120M increase in its base budget, but it had a $96M decrease in purchasing power that coincided with the end of Cancer Moonshot funding. Another aspect is emerging opportunities, which NCI prioritizes and funds, including The Cancer Genome Atlas (TCGA) and the RAS Initiative.

Dr. Lowy provided an overview of the Research Project Grant (RPG) pool and changes in grant applications to NCI over time. He first noted that NCI funds many critical components of cancer research through mechanisms outside the RPGs, including SPOREs, Cancer Center Support Grants (CCSGs), cancer training, and clinical trials networks. From FY 2013 to FY 2023, both the rate of applications and number of applicants to NCI increased substantially, more than for other NIH institutes and centers. The percentage of NCI modular awards (up to $250,000 in direct costs) has progressively decreased from 63 percent in FY 2012 to 14 percent in FY 2023. The NCI decreased the budgets of these awards by 8.5 percent, amounting to $225,000 in direct costs. During this same period, the number of NCI non-modular awards (greater than $250,000 in direct costs) increased from 38 percent to 83 percent.

From FY 2016 to FY 2023, for experienced investigators, the payline was at the 10th percentile in FY 2016, decreased to the 8th percentile in FY 2019, returned to the 11th percentile in FY 2021, and then remained stable. The number of awards from unsolicited applications increased to more than 800. During this same period, NCI increased paylines for ESIs R01/R37 by 5 percent, resulting in an increase from the 12th to 17th percentile. The outcome has been an increase to funding more than 120 ESIs yearly, and this trend is expected to continue.

Dr. Lowy discussed the possible impact of a constrained budget on NCI activities. He highlighted areas NCI can consider prioritizing, including developing new standards of care, rather than research to increase uptake of current standards of care or decreasing the number of CCSGs, Cancer Centers, or SPORE grants. NCI will have hard decisions to make when establishing priorities among developing new standards of care, reducing the investments in requests for applications (RFAs) to protect new investigator-initiated research, funding noncompeting RPG awards at less than 100 percent of the commitment level, and maintaining the number of extramural trainees through specific trainee award mechanisms.

Questions and Answers

In response to a question from NCAB Chair Dr. Carpten about the single–principal investigator (PI) and multi-PI awards, Dr. Diane Palmieri, Center for Research Strategy, NCI, confirmed that multi-PI awards were primarily modular awards.

Dr. Ashani T. Weeraratna, Bloomberg Distinguished Professor of Cancer Biology, E.V. McCollum Chair of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Co-Program Leader, Cancer Invasion and Metastasis Sidney Kimmel Cancer Center, Johns Hopkins School of Medicine, asked about the continuance of the SPORE program, especially since NCI and NIH Directors have mentioned that this may not be a sustainable program. Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis (DCTD), and Associate Director, Translational Research Program, remarked that overall, the SPORE program is healthy and that the research outcomes have been amazing. A 2015 evaluation of the program was favorable, and the reviewers suggested areas for improvements, which NCI has incorporated. Although seven SPOREs have been discontinued because of budget cuts, NCI is hoping this will not reflect the future. She also called attention to the companion RFA to the SPORE program, the Cancer Health Disparities and Minority Health (CHD-MH) SPORE. The applications are due the end of September, and the response appears to be robust. NCI has completed 25 preapplication CHD-MH SPORE consultations with interested research groups. Dr. Hecht emphasized that the DCTD/NCI has established collaborations between the SPOREs and industry, which now has allowed for the development of new agents in the clinic.

Dr. Carpten asked about indirect costs and the percentage of the NCI budget supporting these costs. Mr. Ricks noted that NCI does fund the indirect costs but could not immediately specify the percentage of NCI budget allotted for indirect costs. He explained that the indirect rates often are managed by an organization outside NIH's control. Dr. Lowy added that 60 percent of the R01 expenses represents direct costs, and the remainder is indirect costs.

Ms. Anderson suggested investigating approaches for informing Congress about the underfunding of critical NCI programs, which encompass indirect costs of grants, and to review similar methods used by the Alliance for a Stronger FDA, for example.

V. LEGISLATIVE REPORT—MS. M.K. HOLOHAN

Ms. M.K. Holohan, Director, OGCR, reported on the FY 2025 appropriations, congressional calendar, legislative issues to watch, and engagement and advocacy activities.

FY 2024 ends in 26 days, and the FY 2025 appropriations bills are still in progress. A continuing resolution (CR) likely will be needed to fund the government and may extend until after the federal elections. House Speaker Michael Johnson announced a 6-month CR that would run through March 2025 and is attached to the Safeguard American Voter Eligibility (SAVE) Act. This Act would prohibit noncitizens from voting in federal elections, which already is illegal. The House passed the SAVE Act in July 2024. Whether the lame-duck 118th Congress, which runs through December, can complete the

appropriations is uncertain. Ms. Holohan explained that deferring appropriations into March would leave the FY 2025 budget for the 119th Congress to decide.

The bill out of the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS) was not a bipartisan bill. It has a topline level below the FY 2024 enacted levels and proposes flat funding for NIH ($48B), a $651M increase for NCI, and a $1B reduction in funding for the Advanced Research Projects Agency for Health (ARPA-H). The proposed increase for NCI is a result of proposed restructuring within NIH. The bipartisan Senate Labor-HHS Appropriations Subcommittee bill has a topline level above the FY 2024 enacted levels and proposes a $2.3B increase for NIH ($50.35B), a $266M increase for NCI, and flat funding for ARPA-H. Ms. Holohan remarked on the strong bipartisan support for cancer research, which has benefited NIH, NCI, academia, the cancer research community, patient advocates, and cancer organizations.

Ms. Holohan briefly reported on the congressional calendar. Congress was on recess in August, and the time when both chambers are in session is limited. Their first activity will be to pass a CR and other legislation to be decided in September 2024. Congress also has expressed interest in discussing AI legislation. Election Day is November 5, and the lame-duck Congress begins November 12 and runs through December. The outcome of the elections will determine what can be completed during this period.

Ms. Holohan noted "must-pass" legislation that requires approval before the current Congress expires in September 2024. These bills include a new Agricultural Improvement Act (commonly known as the Farm Bill) and the National Defense Authorization Act for FY 2024. She also highlighted "may pass" legislation, which includes bills related to telehealth extension, drug shortages, clinical trials and access, AI, and NIH-specific legislation, such as the 21st Century Cures Act 2.0.

Regarding cancer research, engagement, and advocacy, Dr. Rathmell has met with many members of Congress to discuss NCI's cancer research activities. In July 2024, she attended and provided brief remarks during the National Brain Tumor Society reception and met with Rep. Roger Williams (R-Texas) and Rep. Susan Wild (D-Pennsylvania). Dr. Rathmell also visited The University of Kansas Cancer Center at the invitation of Senator Jerry Moran (R-Kansas). She also visited The University of Chicago and had an opportunity to meet with Senator Richard Durbin (D-Illinois).

VI. RECOGNITION OF RETIRING NCAB MEMBERS—DR. W. KIMRYN RATHMELL

On behalf of NCI, Dr. Rathmell recognized the contributions made by NCAB members whose terms have ended. She expressed appreciation for their service and dedication during the course of their terms. Those retiring NCAB members are **Dr. Anna D. Barker,** Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California; **Dr. Howard J. Fingert,** Vice President, Medical Oncology, ONO PHARMA USA, INC.; **Dr. Nikan Khatibi,** Chief Executive Officer and Medical Director, Ahura Healthcare Corporation; and **Dr. Susan Thomas Vadaparampil,** Associate Center Director, Community Outreach, Engagement, and Equity, Professor, Department of Health Outcomes and Behavior, Moffitt Cancer Center.

With the retirement of some NCAB members, NCI welcomed four new NCAB members: **Dr. Callisia N. Clarke**, Chief, Division of Surgical Oncology, Associate Professor of Surgery, Department of Surgery, Medical College of Wisconsin; **Dr. Karen M. Emmons,** Professor, Department of Social and Behavioral Science, Harvard T.H. Chan School of Public Health; **Ms. Tamika Felder,** Chief Visionary, Cervivor, Inc.; and **Dr. Edjah K. Nduom**, Daniel Louis Barro Endowed Chair, Associate Professor, Department of Neurosurgery, Emory University School of Medicine, Brain Tumor Disease Leader, Winship Cancer Institute.

VII. NCI'S SUPPORT OF EARLY CAREER CANCER INVESTIGATORS—DRS. OLIVER BOGLER, JESSICA M. CALZOLA, AND BEHROUS DAVANI

Dr. Oliver Bogler, Director, Center for Cancer Training (CCT), NCI, explained that the mission of training in CCT and CCHE is derived from the NCP and the workforce goal and NCI general mission. Dr. Bolger provided an overview of CCT's training efforts.

Overview of CCT. The CCT consists of three groups: Cancer Training Branch (CTB), which is focused on extramural activities, and the Office of Training and Education (OTE) and Intramural Diversity Workforce Branch, both focusing on intramural activities. The CCT, in collaboration with CCHE, offers a variety of funding opportunities and funding mechanisms across the early stages of the cancer research career. The most active training mechanisms in terms of investments and number of recipients are the Mentored Clinical Scientist Research Career Development Award (K08) and the Ruth L. Kirschstein National Research Service Award (NRSA) (T32). The career transition awards include the NIH Pathway to Independence Award (K99/R00) and the NCI Predoctoral to Postdoctoral Fellow Transition Award (F99/K00). In FY 2024, the CCT received a 5-percent increase in its funding, which amounted to $10 M. This increase supported stipends for early career investigators and increased funding for some mechanisms.

Updates from the CTB/CCT. Dr. Bogler reported updates from the CTB, which is led by Dr. Nastaran Zahir. From FY 2018 to FY 2023, the K08 awards steadily increased, reflecting a strong commitment to physician-scientists. CTB anticipates granting 43 competitive K08 awards in FY 2024. The trend was similar for the T32s and CTB anticipates making 32 competitive T32 awards, of which the majority will be competitive renewals. The success rates for the T32s were 40 percent (averaged over the past three fiscal years) and 25 percent for the K08s. As of February 2023, 45 percent of the recipients supported by the CTB portfolio had an M.D. degree and were concentrated in the Ruth L. Kirschstein NRSA for Individual Predoctoral M.D./Ph.D. Degree Fellows (F30) and K08 mechanisms.

Recent Changes in CCT Training. A new NCI Mentored Research Scientist Development Award (K01) was created and launched that focuses on the mission areas of the DCP and DCCPS. CTB/CCT evaluated one of its flagship transition awards, the K99/R00, and the results were published in the May 2024 edition of the *Journal of Cancer Education*. Two key findings were that K99 awardees do well with securing downstream funding, such as R01 and equivalent, and that awardees competed well in the job market, such that 95 percent transitioned to independence. The K99 award did not accelerate toward independence. The purpose of the original design of the K99 was to accelerate investigators to independence, but data show no difference in the time between the Ph.D. and a first R01 for those receiving this award. Dr. Bogler attributed this to the window's being closer to when ESIs apply for their first R01, which is 10 years.

CCT/NCI made a minor change to the K99 program to expand the eligibility from 4 years of postdoctoral experience to 6 years. This change provides postdoctoral fellows more time to further their research and strengthen their grant proposals. NCI will soon release its own K99/R00 program announcements with special receipt, referral, and/or review (or PAR). With the implementation of this change, NCI plans to sunset the CCT Career Development Award (K22), which allowed up to 8 years of postdoctoral experience and is equivalent to the R00 phase of the K99/R00.

The OTE, led by Ms. Erika Ginsburg, published a report on the Sallie Rosen Kaplan Postdoctoral Fellowship for Women Scientists in Cancer Research in the June 2024 edition of the *Journal of Cancer Education.* The report highlighted that this leadership training program for intramural postdoctoral women scientists has a tremendous impact on their careers, self-confidence, and agency and on their ability to secure positions in cancer research.

Dr. Bogler noted that CCT supports roughly 1,000 investigators in the Intramural Research Program and has reach to another 1,000 grantees through its training grants and other funding mechanisms. Therefore, CCT launched two products: a podcast, *Inside Cancer Careers*, to illuminate the different careers in cancer research, and NanCI, an AI-powered application (app) designed to help early career scientists manage the literature and make social connections.

CCHE: Diversity Training Overview. Dr. Behrous Davani, Branch Director, Diversity Training and Biomedical Workforce Development Branch, CCHE, NCI, summarized the programs and initiatives in the training space supported by CCHE. These efforts are aligned with the empowering goals of the NCP, which are optimizing the workforce, engaging every person, and eliminating inequalities. CCHE's flagship program is the Continuing Umbrella of Research Experiences (CURE) Program. CURE aims to support a continuum of competitive funding opportunities for individuals from middle school through early-stage investigator and includes both institutional and individual awards. CURE is a pathway program that focuses on cultivating a culture of excellence, creating a pathway for progress, and fostering a sense of belonging and community among the trainees and investigators. This holistic approach includes enhanced professional development opportunities, mentored mock review, professional development workshops, peer mentoring, and navigation of trainees.

Dr. Davani described the purpose of each funding mechanism within the CURE pathway and the trends observed in the last 10 years. The Research Supplements to Promote Diversity (Diversity Supplements) program trains and provides career development for individuals from high school to ESI level. The supplements often serve as the gateway for investigators to enter the NCI research community. In FY 2024, CCHE received 218 Diversity Supplement applications and awarded 180. The Ruth L. Kirschstein NRSA (F31) Diversity Predoctoral Fellowship was developed to support mentored research training leading to a Ph.D. or dual doctorates. F31 applications significantly increased from FY 2015 to now, and these applications received high impact scores. CCHE's career development portfolio includes three mechanisms (K01, K08, and K22), and applications received increased 21 percent.

A portfolio analysis of the K awards revealed that 36 percent secured R01 funding after the K award ended. The R21 Exploratory Grant Award to Promote Workforce Diversity in Basic Cancer Research, co-sponsored with CCHE by the Division of Cancer Biology, assists new investigators and ESIs who have not received an R01. The R21 applications decreased over the years, likely due to the competitive environment and stringent payline. The R25 YES program began in 2017 and engages middle school, high school, and undergraduate students and their teachers in cancer research, education, and outreach activities. Since its inception, 2,500 students and teachers have participated in R25 activities; 24 R25 YES programs are active across the country.

From FY 2019 to FY 2023, 34 percent of CURE awardees were African American/Black and 50 percent were Hispanic-Latino. Some programs, such as R25 YES, have significant representation from other minority groups, including American Indian and Alaska Native (14 percent) and from low socioeconomic backgrounds or rural areas (23 percent). Much of the CCHE portfolio is in basic science cancer (59 percent), followed by social and behavioral sciences (18 percent) and translational and clinical sciences (17 percent and 6 percent, respectively). Less than 20 percent of the CURE portfolio focuses on cancer health disparities. CURE continues to attract a diverse pool of competitive researchers and physician-scientists. Except for the R21s, the number of applications received and awards issued for FY 2024 has increased compared with FY 2023, but NCI could not support all meritorious applications due to budget constraints.

Dr. Jessica M. Calzola, Branch Director Innovative Programs Branch, CCHE, NCI, described two signature programs for ESIs. In 2018, in collaboration with multiple divisions, offices, and centers within NCI, the intramural CURE (iCURE) was launched. iCURE supports qualified individuals from diverse

backgrounds to train with investigators within NCI. Participants are matched with research mentors within the NCI research enterprise, and they are supported in their career development by being matched with mentors outside their research groups. More than seven cohorts have supported 105 scholars, 10 of whom are onboarding this week. The Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program is an NIH Common Fund Program. NCI manages the Faculty Cohort Program, which has three goals: address culture within the institutions that were funded, recruit diverse cohorts of faculty, and provide those faculty with an environment of support that accelerates their career. Of the 181 faculty awardees expected to be onboarded through FIRST, at least 25 will focus on cancer research. To date, 15 of the awardees have been recruited, i.e., those who have a cancer focus to their research and who are potential future applicants for NCI's RPG pool.

Questions and Answers

Dr. Karen M. Winkfield, Executive Director, Meharry-Vanderbilt Alliance, Ingram Professor of Cancer Research, Professor of Radiation Oncology, Vanderbilt University School of Medicine, commended NCI on the efforts to support the next generation of researchers through the CCHE programs. She asked about the diversity of the recipients and applicants to the program. Dr. Bogler noted that representation of minorities in the K99 portfolio is not where it should be, but data are limited. He also noted that assessing diversity in these awards at the institutional level also is a challenge because they are open competitions, and the largest institutions tend to consume most of the resources in the Cancer Training Branch, with several having six or more T32 grants from NCI. The F99/K00 mechanism is more restrictive, and institutions can only submit one candidate for this award. Discussions are ongoing within NCI on how to address these issues. Dr. Winkfield suggested reviewing the number of awards given to institutions that have high endowments and built infrastructure for capacity in place compared with institutions needing such funding and infrastructure.

In response to a question from Dr. Hayes Dixon about the success of the K99/R00 awardees transitioning to non-grant-supported positions, Dr. Bogler explained that the majority of K99/R00 awardees transition into academic positions and successfully move to the R00 portfolio. Roughly 5 percent transition into industry.

Dr. Barker emphasized training the next generation of NCI investigators in basic and complex mathematics in preparation to support NCI's AI and cancer research efforts. Dr. Bogler called attention to current activities in this area, including the *Inside Cancer Careers* podcast and a recent episode on AI and cancer research to engage the potential next generation of cancer researchers who are training to be mathematicians. The opportunity exists for NCI to develop some additional pathways and mechanisms for bringing people from those disciplines into the cancer field, but the time is not ideal to launch new programs. Dr. Barker suggested partnering with companies that have similar needs in health care, such as Google Health. Dr. Bogler added that NCI's mobile app, NanCI, is being developed in collaboration with Google.

Dr. Davani underscored that NCI cannot achieve its goals alone and will need assistance from the Cancer Centers to focus on NCI programs and on ways to diversify the cancer research workforce. NCI also may need to partner with the private sector to focus on these areas. NCAB Chair Dr. Carpten spoke on rebalancing the portfolio rather than just focusing on new programs.

Dr. Nduom reflected on his experience participating in NCI training programs through mid-career and expressed concern in the current landscape regarding diversity. He suggested monitoring diversity statistics in NCI's successful programs, including the training grants. Dr. Bogler pointed out that K99 applicants have tended to model their mentors or research laboratory peers who have previously received this award; he noted that this model may not exist at many institutions and could partly explain the lack of a diverse pool of applicants from a more diverse body of institutions. Partnerships between established

institutions and those that do not have a history of applying for these particular mechanisms would be beneficial. In addition, the Cancer Centers could help their community peers with their outreach efforts and applying for K99 awards.

NCAB Chair Dr. Carpten commented that significant investments have been made at many minority-serving institutions to build infrastructure appropriately, but more work remains to be done. He suggested expanding the research portfolio to include digital-based research in data analysis, informatics, or advanced digital technology at the Ph.D. level of training.

Dr. Luis Alberto Diaz, Jr., Head, Division of Solid Tumor Oncology, Grayer Family Chair in Medicine, Department of Medicine, Memorial Sloan Kettering Cancer Center, commented that the predictors of success can be best measured at the high school and college levels because learning about AI or novel techniques when in medical training or as a postdoctoral fellow may come rather late. He encouraged bolstering training earlier in the funding process, which could potentially yield results. Dr. Calzola noted that a common element of success for postdoctoral fellows is mentorship, regardless of the training program. Dr. Davani added that the R25 YES program starts from middle school and noted that some projects focus on data science and AI.

VIII. CHILDHOOD CANCER DATA INITIATIVE (CCDI)—DRS. BRIGITTE C. WIDEMANN, SARAH E.S. LEARY, AND DIANA L. THOMAS

Dr. Brigitte C. Widemann, Chief, Pediatric Oncology Branch (POB), Head, Pharmacological and Experimental Therapeutics Section, Senior Investigator, and Special Advisor to the NCI Director for Childhood Cancer, provided an update on the CCDI and the Molecular Characterization Initiative (MCI). MCI collaborators will present their findings later in the presentation.

About CCDI. The CCDI started in 2020 and has made significant progress. The aim is to build a community centered on childhood cancer care and research data, with the aspirational goal of learning from every patient with cancer. The key goals are to gather data from every child, create a national strategy from diagnosis to treatment, and develop a platform and tools of clinical and research data to improve treatment, quality of life, and survivorship, all by engaging the entire childhood cancer care and research community. The CCDI Hub provides an entry point for researchers, data scientists, and anyone interested in analyzing pediatric cancer data. Several data types are available for analysis to provide a source for new discoveries that may affect lives.

CCDI MCI. The MCI is a national strategy for appropriate clinical and molecular characterization for every child with cancer. It provides state-of-the-art molecular characterization of cancers for as many as 3,000 children annually and builds a clinically annotated biobank for future research. MCI is a partnership between NCI and the Children's Oncology Group (COG) Project:EveryChild. A child with a newly diagnosed cancer can enroll in the MCI protocol and undergo state-of-the-art sequencing of the tumor and germline testing. Results are returned to participants and treating physicians within 2 to 3 weeks. All data, including pathology data, are deposited in the CCDI Data Ecosystem and are available for analysis. Since March 2022, the MCI has enrolled more than 3,000 participants with pediatric brain tumors. Current cancer types include newly diagnosed central nervous system (CNS) tumors, soft tissue sarcomas, rare tumors, and neuroblastoma at risk. Future enrollments will include participants with Ewing sarcoma and those with relapsed tumors.

MCI CNS Cohort: Overview. Dr. Diana L. Thomas, Operations Director, Anatomic Pathology Biopathology Center, Nationwide Children's Hospital, provided an overview of the MCI CNS cohort, including enrollment and demographics, and summarized the initial results, including diagnostic testing. She noted that Project:EveryChild maintains a childhood cancer registry and biobanking study of children

and young adults with cancer. It is the initial mechanism by which patients consent and enroll for participation in the MCI.

The CNS cohort data includes 2,170 participants with CNS tumors who enrolled in MCI between March 2022 and December 2023. Approximately 50 percent of participants enrolled during the first 20 months of the study were registered in large institutions with high enrollment rates, and 50 percent were from smaller institutions, with much lower enrollment rates. The CNS cohort continues to grow and as of today includes more than 3,000 patients.

Approximately 90 percent of MCI participants live in the United States; many were enrolled in COG-affiliated hospitals, and many residing in rural areas traveled to receive care. The CNS cohort has a median age of 9 years, with slightly higher male participation. The race and ethnicity of participants who enrolled at U.S. COG sites was similar to the U.S. Census Bureau race and ethnicity data. By CNS tumor diagnosis category, the highest enrolling categories are low-grade gliomas, high-grade gliomas, and medulloblastoma. Although current or historical clinical trials have been available for some of these patients, many rarer tumors are presented in the MCI cohort, for which no clinical trials have been available to date.

In the practice of pediatric pathology in 2024, CNS tumors require molecular characterization to inform an integrated diagnosis. The three assays that are part of MCI's somatic diagnostic testing are performed in a College of American Pathologists– or Clinical Laboratory Improvement Amendments–certified setting: DNA methylation, targeted whole-exome DNA sequencing, and Archer fusion panel. All CNS patients who have undergone MCI testing to date have received clinical reports with at least one clinically meaningful result. The results showed molecular diversity of tumors with frequent clinically relevant molecular findings. Dr. Thomas emphasized that the broad tumor characterization through the MCI allows rare diagnoses not to be missed that, for example, require methylation profiling for definitive classification, while also further refining diagnoses for accurate risk stratification and therapy selection.

MCI also includes germline testing, which has implications for additional screening for patients and their families. Approximately 12 percent of patients tested have been found to have genetic cancer predisposition, involving 49 different genes. The most common genes have germline mutations of around 1 percent frequency, indicating that this broad testing approach is critical to identifying many of these genes. More focused testing through immunohistochemistry, for example, would have missed these results. The MCI CNS data also include site-reported follow-up on participants. A large proportion of study sites have confirmed that MCI testing has helped refine their diagnosis and matched their initial therapy based on the sequencing results. MCI results are also being used for clinical trial enrollment. Dr. Thomas explained that this is a large cohort of children included in MCI with rare CNS tumor diagnoses, for whom trials are not available. She closed by noting that the clinical community is in a period of transition, in which molecular information is being incorporated into clinical trial design.

MCI CNS Cohort: Clinical Trial Design. Dr. Sarah E.S. Leary, Attending Physician and Medical Director, Pediatric Brain Tumor Program, Professor, Department of Pediatrics, University of Washington School of Medicine, discussed additional results, focusing on the diagnoses of the various tumors. She highlighted how MCI has affected the cancer community's ability to appropriately diagnose, risk stratify, and treat pediatric and young adult patients with CNS tumors, as well as guide clinical trial design.

Medulloblastoma is the most common malignant tumor of the CNS, and it has four distinct molecular groups that require extensive testing for proper characterization. Clinical and molecular risk factors were used to categorize tumors and select the appropriate intensity of therapy. The DNA methylation test best describes the four groups. Exome sequencing is used to identify small point mutations and indels. Exome copy number is used for both high- and low-risk factors.

Dr. Leary described the COG clinical trial design of integrated clinical and molecular risk stratification. A medulloblastoma clinical trial is open for both low- and average-risk medulloblastoma, and two studies are being developed for high-risk disease, in both older and younger children. Dr. Leary noted that this design is the most complicated risk stratification and required MCI participation because it is the only test available to provide the broad, consistent information needed for trial design. She pointed out that of the 400 children with medulloblastoma enrolled in the MCI in the first 20 months, most did not go on trial because no trial had opened. In the first year of the MCI, it is estimated that more than half the children in the United States are using the MCI for their clinical testing. Other trials have opened and have required less complicated molecular characterization. These include the high-grade and low-grade glioma trials, which are evaluating kinase inhibitor therapy and require both positive and negative selection of specific genes.

Diffuse midline glioma remains one of the last of the incurable pediatric cancers and is defined by a mutation in the histone gene, which was discovered from autopsy studies. With advancing surgical techniques, these tumors can often be diagnosed with molecular characterization and biopsy. MCI testing showed that this tumor is the most common high-grade glioma observed in pediatrics. As expected, the first-year follow-up data showed 43 percent survival, with more than half the children succumbing during the first year after a diagnosis. Without improvement in therapy, most of the children will succumb to disease by the third year.

Dr. Leary highlighted that the MCI testing revealed additional mutations that are potentially targetable with new therapies or therapies that already exist for other diseases. Specific mutations have been observed that co-occur with diffuse midline glioma in other COG therapy trials evaluating common mutations (e.g., *BRAF* V600) and with sequencing, several other mutations with potential therapeutic implications have been identified. Dr. Leary and her laboratory have observed mutations in the 5 to 10 percent range in their analysis of the MCI data, which have potentially known therapeutic implications. They observed fusion proteins in 7 of the 86 initial patients enrolled in MCI, which have clear implications for potentially effective therapeutics. They also identified germline mutations (e.g., *PMS2*) in patients with diffuse midline glioma, which has implications for checkpoint inhibitor therapy.

Building on the MCI, Dr. Leary noted studies for the next phase, such as observing cancer predisposition and following up on the children identified with cancer predisposition and their families. The MCI/CCDI is working to connect to other robust clinical data sources, supporting additional genomic discovery, and supporting clinical research in ultra-rare tumor populations.

CCDI Coordinated Pediatric, Adolescent, and Young Adult Rare Cancer Initiative. Dr. Widemann informed NCAB that this initiative is building on the unmet need for patients who have ultra-rare tumors, where the standard of care does not exist and clinical trials are not feasible. NCI is developing a CCDI coordinated effort that will provide the infrastructure to study multiple rare tumors simultaneously. Any institution in the country can participate.

The objective is to evaluate the feasibility of a national, longitudinal observational study for children and adolescents and young adults (AYA) with rare cancers. Data collection will include medical records, imaging, and pathology; molecular characterization through MCI; common data elements; and patient-reported outcomes. Common data elements being considered include demographics, disease and treatment, tumor pathology and genomics, tumor response, family history, and follow-up. In July 2024, NCI hosted a common data elements workshop, and the outcomes are informing this work.

The next steps will be to finalize the common data elements and patient-reported outcomes, finalize the protocol, and begin study enrollment in 2025. To join the study, a child or AYA must be diagnosed with a rare solid tumor. All participants will be enrolled in the CCDI MCI. The study is expected to expand to investigation of blood cancers.

Questions and Answers

Dr. Hayes Dixon asked about plans for increasing the number of participants enrolled in the trial and communicating the molecular characterization differences to investigators external to the COG network. Dr. Widemann explained that NCI is discussing increasing enrollment and that a key requirement will be that patients who enroll in the trial have a doctor who receives the results. NCI will extend an offer to help physicians communicate the molecular results, especially to those in more rural settings who might not be able to interpret the findings as well.

In response to a question from Dr. Hayes Dixon about whether the remaining funding is sufficient to accomplish the data collection goals, Dr. Widemann inferred that to overwhelm the CCDI data system, enrollments in these rare cancers would have to significantly increase, which would be a good problem to have in terms of identifying new treatments. She agreed that data collections for all children with rare tumors could tax this system. NCI will be closely monitoring enrollments.

Dr. Nduom observed data suggesting that the cerebrospinal fluid (CSF) does not necessarily reflect tumor genomics in most cases. He pointed out that the adult brain tumor community is emphasizing the need to aggressively collect and interrogate multiple tissue samples to better understand tumor genomics and make progress for treatments and that they are publishing position statements to support this approach. He asked about a similar approach for pediatrics, given the ethical concerns and genomics. Dr. Leary explained that collecting sequential molecular information also has been a challenge in pediatrics. Several position statements, in addition to research published on this topic, might be needed for the tumor biology field to better understand about CSF and brain tumors. With new techniques, including sequencing within CSF, new mutations are being identified, especially in diffuse midline glioma. Most tumors are not completely resected, and biopsies will miss the identifications. Mutations can be detected without positive cytology in the CSF. Investments in new technology will be critical.

NCAB Chair Dr. Carpten commented on the opportunity to collect pediatric tissue samples to build a living biorepository to inform future studies of the biology of pediatric rare cancers. He also noted the opportunity to expand to advanced technology, such as single-cell spatial transcriptomics to better understand the tumor microenvironment and to stratify clinical parameters by race and ethnicity, and perform genetic similarity or genetic ancestry analysis in the MCI CNS cohort. Dr. Leary commented on potential MCI resources for others in the CNS community, including developments from a cancer predisposition project that will focus on constitutional genomics for CCDI data.

Ms. Grant was unclear why major metropolitan areas like Boston and San Francisco were not the largest sources of patient samples. She asked about institutions already performing genomic testing in house before the MCI and plans for integrating the CCDI genomic data into TCGA. Dr. Leary clarified that some high-enrolling clinical sites do genomic testing as part of their clinical research and that other sites are prioritizing tests to support a diagnosis. Her understanding is that pediatric CNS tumor data have not been included in the TCGA.

Dr. Leary clarified that such genetic counseling is organized through the COG and that fewer questions are being received, and that they extend beyond the basic queries about the meaning of the results. Returning results to the treating physician establishes and strengthens the doctor–patient relationship. Most community oncologists practicing in rural areas have established and work within their networks to answer their questions. NCAB Chair Dr. Carpten added that Patient Engagement and Cancer Genome Sequencing Initiative, which is a Cancer Moonshot–funded project, is conducting similar clinical activities, such as returning results and counseling.

In response to comments about genetic counseling and germline mutations in the MCI CNS cohort, Dr. Widemann noted plans in the Rare Cancer Initiative to establish cohorts to monitor patients

with cancer predispositions. They also are considering establishing national or international clinical and molecular tumor boards to assist patients who may not have access to counselors or may need advice or recommendations about treatment decisions.

IX. OVERVIEW: NCI AND ARTIFICIAL INTELLIGENCE (AI)—DRS. WARREN A. KIBBE, JULI KLEMM, AND ISMAIL BARIS TURKBEY

Overview of NCI and AI. Dr. Kibbe provided an overview of NCI's AI activities. He began by noting that, as the NCI Deputy Director for Data Science and Strategy, he is responsible for advising the NCI Director and other senior leaders on data use, stewardship, and sharing, as well as providing strategic direction to the NCI CBIIT. He expressed his enthusiasm for integrating NIH's AI-related strategic directions into NCI activities, informing HHS directions regarding data science, and providing counsel across NCI and NIH initiatives.

Dr. Kibbe emphasized that AI has been a topic of interest for centuries, and mathematicians began developing modern logic models for AI approaches in the 1960s. Modern capabilities for computation have led to large language models, such as ChatGPT, that have transformed how people think about AI, especially in their daily lives. He emphasized the importance of considering AI readiness, trust and ethics, and diversity. Humans must be engaged in decision-making and trained in the use of new tools. Large technology companies are generating new AI models and algorithms, and these developments offer opportunities for new advances in cancer research. Dr. Kibbe underscored the importance of considering the AI landscape as an ecosystem.

The NCI Artificial Intelligence Working Group. Dr. Juli Klemm, Program Director, Center for Strategic Scientific Initiatives (CSSI), NCI, discussed the NCI Artificial Intelligence Working Group. She explained that AI refers to a broad collection of computer methods that can learn patterns in data that mimic the human brain. These methods are increasingly being applied by cancer researchers and clinicians across the whole spectrum of cancer research, including cancer screening and diagnosis, drug discovery, cancer surveillance, and health care delivery.

NCI has embedded elements of AI across its portfolio of grants and contracts as cancer researchers are increasingly using these methods in their research activities. In 2020, NCI established the NCI Artificial Intelligence Working Group to provide a hub for communication and coordination of AI-related scientific projects and programs both across NCI and outside of NCI and identify NCI-wide cancer research opportunities that could most benefit from the appropriate use of AI. Today, this working group consists of almost 30 members representing nearly all of NCI's divisions, offices, and centers.

The Working Group coordinates NCI's participation in broader NIH AI activities, particularly those coordinated by the NIH Office of Data Science Strategy (ODSS), as well as NIH Common Fund activities (e.g., Bridge to AI). The Working Group also serves as a resource to provide support for communications, congressional briefings, and other AI-related inquiries that NCI receives. Furthermore, the working group participates in broader federal activities, including the AI components that are embedded in the Cancer Moonshot initiative, ARPA-H, the National Science Foundation, and broader HHS activities.

Other NCI activities include hosting forums and workshops on emerging topics in AI for cancer research, coordinating participation in AI-related funding opportunities, hosting a prize challenge on evaluating the data in the Cancer Research Data Commons for AI data readiness, and recognizing the need for increased transparency and understanding of AI models. Dr. Klemm noted that more information on NCI's activities in this space, for both researchers and the public, is available through the NCI website.

CCR Artificial Intelligence Resource (AIR). Dr. Ismail Baris Turkbey, Senior Clinician, Molecular Imaging Branch, and Head, AIR, NCI, spoke on research activities at AIR, which was established in 2020 to develop translational AI models to enhance imaging-based research both within and outside NIH. AIR supports a broad range of both clinical and preclinical research, including radiology, digital pathology, endoscopy, and electronic health records. Dr. Turkbey highlighted an example of AIR's efforts to address inconsistent diagnostic performance of prostate magnetic resonance imaging for detecting prostate cancers. Using intramural and extramural data, researchers developed a cascaded, fully automated model to process the data.

Dr. Turkbey emphasized that these models are designed to be translational, meaning that they can function across clinical and research environments. The model uses Medical Open Network for AI (MONAI), a deployment process that detects sequences and identifies organ segments and cancer-suspicious areas. Dr. Turkbey shared examples of data processing and applications. He noted that the models are open source and have been used by researchers around the world. AIR operates through three tiers: productivity, diagnostic assistance, and discovery. Dr. Turkbey concluded by underscoring the importance of model deployment and training.

Questions and Answers

NCAB Chair Dr. Carpten inquired about partnerships with FNLCR. Dr. Kibbe explained that AIR's partnerships with the U.S. Department of Energy (DOE) also involve FNLCR. Dr. Klemm noted that computational resources for model and data sharing have been established through this partnership. Dr. Carpten also asked about racial and ethnic diversity within the models. Dr. Kibbe explained that AI models can help reduce human bias in this context. Dr. Turkbey added that AIR has access to representative patient populations and is studying outcomes of using AI assistance across groups.

Dr. Winkfield spoke on the importance of workforce diversity and requested additional details on how the AI model is addressing diversity. Dr. Turkbey clarified that the models are appropriately representative of the patient populations. Dr. Klemm added that ODSS is coordinating NIH efforts to think about bias and equity in AI, with a focus on workforce development across academic centers.

Dr. Hayes Dixon also underscored the importance of acquiring diverse data at early stages for equitable deployment (e.g., for skin cancer). Dr. Turkbey noted that federated learning is important for moving models across populations and incorporating diversity.

Dr. Barker inquired about plans to address the need for longitudinal data. Dr. Kibbe explained that the CCDI is pursuing efforts in this area. He agreed on the importance of understanding the trajectory of disease.

Ms. Grant asked about funding for the current data infrastructure. Dr. Kibbe underscored the importance of industry partnerships for funding. Dr. Turkbey added that NCI offers high-performance computing resources for investigators, and laboratories generally have their own infrastructure for developing models.

Dr. Azad suggested organizing workshops focused on AI applications to foster international discussions between academic researchers and private industry. Dr. Kibbe agreed and noted that the Artificial Intelligence/Machine Learning Consortium to Advance Health Equity and Researcher Diversity (known as AIM-AHEAD) program is pursuing efforts in this area and that opportunities for collaboration in cancer research could be pursued.

X. UPDATE: NCI COMMUNITY ONCOLOGY RESEARCH PROGRAM (NCORP) AND THE NATIONAL CLINICAL TRIALS NETWORK (NCTN)—DRS. PHILIP E. CASTLE AND JAMES H. DOROSHOW

NCORP Update. Dr. Castle provided updates on NCORP, which is an NCI flagship program. NCORP was launched in 2014 and merged two community programs: the Community Clinical Oncology Program, which was established in 1983, and the NCI Community Cancer Center Program, which started in 2007. The goals are to enroll patients in treatment and advanced imaging clinical trials that are developed through the NCTN by the DCTD and to support inclusion of health-related quality-of-life correlative studies in NCTN treatment trials. In 2022, the United States had 18 million cancer survivors, which was more than 5 percent of the U.S. population. By 2040, it is estimated that this number will increase to 26 million cancer survivors, or 7 percent of the U.S. population. Approximately 1 in 14 people will be a cancer survivor. To that end, NCORP aims to engage large and diverse patient populations receiving care in the variety of community oncology settings and generate a broadly applicable evidence base that contributes to improved patient outcomes and reduction in cancer disparities.

Dr. Castle paused to honor and reflect on the life of Dr. Worta McCaskill-Stevens, former Director of NCORP and Chief, Community Oncology and Prevention Trials Research Group, DCP, NCI, who made seminal contributions to NCI over an illustrious career. NCI hopes that Dr. McCaskill-Stevens' legacy will continue to grow through the NCI Worta McCaskill-Stevens Career Development Award for Community Oncology and Prevention Research, which was established by then–NCI Director Dr. Monica M. Bertagnolli. He acknowledged Acting NCORP Director and Acting Chief, Community Oncology and Prevention Trials Research Group, Dr. Brandy Heckman-Stoddard, and expressed his appreciation for her stepping in to fill these roles.

NCORP consists of 7 Research Bases, 32 Community Sites, 14 Minority/ Underserved Community Sites, and more than 1,000 clinical practice locations. Fifty percent of the NCORP sites have affiliate sites, thus extending services across the entire United States. Key attributes of NCORP are its people, including more than 4,000 physician scientists and nearly 5,000 research staff; health care systems, including stand-alone facilities; affiliates and subaffiliates; and types of clinical sites. NCORP works closely with the NCTN, leveraging infrastructure, such as the Central Institutional Review Board and Metadata Rave. The NCTN focuses on late-phase treatment trials and advanced imaging, whereas NCORP focuses on cancer control, including symptom management, quality of life, cancer prevention and screening trials, and cancer care delivery, which are the activities of DCP and DCCPS. Over the past five NCORP fiscal years, which begins in August and is different from the federal government's fiscal year, NCORP supported various treatment, screening, and prevention trials and contributed to the accrual of more than 3,000 participants to treatment trials alone. By trial type, the majority of accruals were attributed to the Tomosynthesis Mammographic Imaging Screening Trial (or TMIST). NCORP contributes 25 percent of the minority accruals in treatment trials.

Dr. Castle summarized study development in NCORP. For Research Base concept development, investigators, along with the Research Base Working Groups, develop a concept that is vetted by other researchers and community members and then approved by the Research Bases. The concept is submitted to the NCI and the NCORP Steering Committee for review. If approved, the concept advances to protocol development. The process is similar for externally funded studies for which investigators have their own funding; leveraging the NCORP infrastructure can potentially reduce the overall cost of these studies.

The 2015 symptom management and quality-of-life strategic priorities align with NCI's strategic planning process. The first-tier high-priority areas include cognitive impairment, neurotoxicity, cardiovascular toxicity, fatigue, and cancer-specific pain. The second-tier areas include sleep disorders,

bone and health toxicity, metabolic toxicity, and psychological stress. Dr. Castle highlighted examples of ongoing and completed symptom management trials in NCORP.

Two large screening trials are active in NCORP. TMIST is a randomized trial evaluating 2D digital mammography versus 3D tomosynthesis mammography over 4 years, with a primary endpoint of reduction in advanced cancers. TMIST is close to meeting its accrual goals. The Five- or Ten-Year Colonoscopy for 1-2 Non-Advanced Adenomatous Polyps (or FORTE) study is focusing on deescalating the follow-up of low-grade adenomas. The DCP implemented new screening trial requirements for study design, recruitment planning, and accrual milestones of all screening trials in response to Clinical Trials and Translational Research Advisory Committee (CTAC) recommendations after encountering challenges accruing to TMIST.

The DCCPS Cancer Care Delivery Research (CCDR) portfolio, which NCORP supports, has 30 approved protocols, and 12 are open to accrual. The studies address a broad range of care delivery gaps, including guideline adherence and health expenditures. Of the 30 approved protocols, 18 are randomized accruals and 13 are practice randomized accruals. As of July 2024, NCORP had facilitated accrual of more than 12,000 patients, nearly 3,000 non-patients, and 839 practices. Minority patient accrual in the CCDR trials averages 23.4 percent.

Regarding the impact of NCORP, Dr. Castle emphasized that NCORP is a community academic partnership that increases the diversity of accrual and generalizability of results. The engagement of community oncologists and the community itself enables faster adoption of the evidence and improved clinical practice and patient care in the community. NCORP focuses on the importance of quality of life and incorporating patient experience and developing interventions to improve the cancer experience and is an NCI-wide collaboration with the DCTD, DCP, and CCHE. He noted aspirations to launch an NCORP incubator program to help new applicants join NCORP.

Dr. Castle asked NCAB for input on expanding NCORP to engage more people in clinical trials; engaging Lead Academic Participating Sites in cancer control and prevention trials and collaborating internationally to conduct these trials; reducing the workload at the sites; enhancing the research impact of trials; connecting data and biospecimens from prior trials to contribute to new research; and helping outside investigators with great ideas to engage with the network.

NCTN Structure and Activities. Dr. James H. Doroshow, Deputy Director, Clinical and Translational Research, Director, DCTD, NCI, updated NCAB on the activities of the NCTN. Dr. Doroshow first expressed appreciation to the many patients who have participated in NCTN trials for more than three decades. Without their participation, there would be no presentation today and major advances would not have occurred. He also expressed appreciation to the health care workers, research nurses, data managers, advocates, investigators, operations staff, and coordinating center staff who have worked tirelessly to make the NCTN a program of national importance.

In 2014, NCI transformed the former cooperative group program's infrastructure into the NCTN to harmonize processes and promote collaborations; focus on questions not well supported in the commercial environment; prioritize trials and incorporate innovative science and clinical trial design; provide large-scale testing of molecularly targeted and defined cancers; and maintain commitment to conduct trials in diverse and special populations. The NCTN consists of six main components: U.S. Group Operation Centers, U.S. Group Statistics and Data Management Centers, Canadian Collaborating Trials Group, Lead Academic Participating Sites, Imaging and Radiation Therapy Core Services Center, and Integrated Translational Science Awards for pilot projects. Under separate RFAs, NCI funds tumor banks for each of the U.S. NCTN groups.

DCTD maintains contracts that support information security, study administration and logistics, clinical data capture and reporting, regulatory monitoring and reporting, audits for data quality and control, and maintenance of correlative science study data. Investigational studies in the NCTN encompass large umbrella or basket trials requiring national catchment areas. These trials currently include the NCI Molecular Analysis for Therapy Choice (NCI-MATCH) successor trials (e.g., Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice), multimodality and non-drug trials, combination therapy trials, and trials involving special populations.

Dr. Doroshow highlighted recent NCTN initiatives. A CTAC working group evaluated the data management profiles of studies that do not require Investigational New Drug (IND) applications, which is 40 percent of NCTN trials. As of 1 January 2025, unnecessary data elements will no longer be submitted in NCTN trials. NCI will evaluate whether this change enhances the ability to accrue and conduct studies more rapidly. Efforts also are focusing on decentralizing NCI trials. Data sharing activities and biospecimen access between the NCTN and NCORP are ongoing.

During the second quarter of 2020, accrual on trials in the NCTN significantly decreased, coinciding with the onset of the COVID-19 pandemic. The NCTN and NCORP implemented changes that allowed greater enhancement and ability for local sites to conduct their trials by telemedicine with FDA approval. Accruals began to recover by the fourth quarter. The NCTN initiated remote consent and remote auditing techniques and began shipping oral agents directly to patients. NCI anticipates that the number of 2024 accruals will reach or exceed the 2021 accruals and resume a trajectory that follows the overall accrual goals of the NCTN.

Most of the accrual in the NCTN is to phase 3 clinical trials, followed by phase 2, and phase 2/3 trials. Because 40 percent of NCTN trials are IND-exempt, the flexibility exists to significantly change clinical trial design and data element reporting to simplify, decentralize, and make accrual easier. More than 60 percent of the pediatric accrual are patients with acute lymphoblastic leukemia. In adult accrual, the major diseases are breast, gastrointestinal, genitourinary, and thoracic lung cancers. Approximately 68 percent of the patients enrolled in NCTN trials are White/Caucasian, and 25 percent are non-White/Caucasian or Hispanic/Latino. The average age of enrolled patients is 65 years, and 16 percent of patients reside in rural areas. Stratifying accrual by project period shows that in period 1 (February 2014–March 2019), screening on study accruals included the Adult and Pediatric NCI-MATCH trials, and period 2 (March 2019–July 2024) intervention accrual decreased by approximately 10 percent because of the COVID-19 pandemic and the closure of the NCI-MATCH trials.

NCTN Key Accomplishments. Dr. Doroshow highlighted key accomplishments of the NCTN. A randomized trial (NRG-GY018) evaluated pembrolizumab combined with paclitaxel and carboplatin in endometrial cancer or recurrent endometrial cancer, and the results showed significant difference in progression-free survival. Data from this trial were used to obtain FDA approval on 17 June 2024 for the use of pembrolizumab in endometrial cancer. This trial, an example of incorporating innovative science and design into clinical trials, is a major achievement for the NCTN.

An NCTN-wide trial (S1826) evaluated the addition of nivolumab or brentuximab vedotin in patients ages 12 to 17 with newly diagnosed advanced stage classical Hodgkin lymphoma. The results revealed that the addition of nivolumab instead of brentuximab vedotin had a major effect on progression-free survival. This study, an example of a collaborative trial in a special population, represents a key step toward harmonizing pediatric and adult therapy for classic Hodgkin disease.

NCI and the FDA collaborated to modernize IND trials and designed the Pragmatica-Lung phase 3 trial (Pragmatica), which leverages the Lung Cancer Master Protocol (Lung-MAP). The goal was to develop a study that is less burdensome for patients and investigators, allows rapid accrual, is representative of a real-world population, and serves as a model for future cancer clinical trials.

Pragmatica was developed in 200 days and is evaluating chemotherapy or a combination of ramucirumab and pembrolizumab in non–small cell lung cancer. The trial was activated on 6 March 2023, with a target enrollment of 700 participants, which was amended to 800. As of 23 August 2024, the trial had reached 87 percent of the initial projected enrollment. Pragmatica could lead to an FDA New Drug Application for this combination and for this large patient population.

In 2023, NCTN investigators reported on a study that evaluated 162 adult NCTN randomized trials since 1980. They found that the experimental treatment from these trials was estimated to have generated 14.2 million additional life-years to patients with cancer, through 2020.

Questions and Answers

Dr. Winkfield asked about the length of time it takes for the review process and to activate a study. She also noted the lack of resources for translation for non-English speakers, which can be a barrier in some clinical trial sites. Dr. Doroshow explained that the CTAC Working Group on Operational Efficiency established guidelines for the timelines for initiating phase 1, 2, and 3 trials in 2014. The timelines were shortened over time but are still unacceptably long, especially compared with industry trials. Dr. Doroshow also pointed out that an electronic Gantt chart that characterizes various components of timelines of NCTN trials is now being maintained. He also noted two contributing factors that have affected trial activation times: the time to receive drug commitments from pharmaceutical companies and, more recently, mandated exceptions due to the COVID-19 pandemic. Dr. Heckman-Stoddard added that NCORP adapted the Working Group on Operational Efficiency guidelines for NCORP trials in 2018. She attributed delays to contracting with companies supporting the trial and not having agents for testing readily available. NCORP, along with PIs, and other investigators, is reviewing timelines of trials yet to be activated to better understand the issues and is shortening times where possible. She pointed out that kickoff calls will be scheduled with the program officer, study PI, project scientist, and Research Base after grants are approved for funding to ensure that duties and responsibilities are clear. Dr. Castle noted that reducing the trial timelines benefits all involved; the current situation underscores the need for an in-depth review of NCTN and NCORP trials to determine where those improvements can occur and will take a collective effort to resolve.

Dr. Christopher R. Friese, Vice Provost, Academic and Faculty Affairs, Elizabeth Tone Hosmer Professor of Nursing, Professor of Health Management and Policy, Associate Director, Cancer Control and Population Sciences, Rogel Cancer Center, University of Michigan, commented on opportunities to ensure more NCORP trials are made available across all research laboratories involved in a study. He asked about the number of NCORP sites that open and actually accrue patients to a study. Dr. Heckman-Stoddard commented that DCP has reported 623 sites open for a specific study; she noted that determining whether a site had accrued participants for a trial was challenging during her initial Research Performance Progress Report review of the NCORP program.

XI. ONGOING AND NEW BUSINESS—DR. JOHN D. CARPTEN

NCAB *ad hoc* Subcommittee on Experimental Therapeutics. Dr. Richard J. Boxer, Clinical Professor, David Geffen School of Medicine, University of California, Los Angeles, Chair of the NCAB *ad hoc* Subcommittee on Experimental Therapeutics, presented the report of the 3 September 2024 meeting. Dr. Boxer noted that the Subcommittee discussed ways to foster collaboration among advocacy groups, academia, private industry, NCI, and the FDA. The fundamental concept is to bring together leaders who discovered, developed, and financed new experimental treatments of cancer. The Subcommittee contemplated why industry, particularly venture capitalists (VCs) that fund industry, is not having conversations and engaging in the innovation at NCI, given NCI's deep experience, expertise, and resources that can accelerate bringing new experimental treatments to patients. The Subcommittee heard a presentation from Dr. Rose Aurigemma, Associate Director, Developmental Therapeutics Program,

DCTD, NCI, and Executive Secretary, on NCI support mechanisms to advance drug candidates. She discussed the interest in new therapies in the public domain and how industry investments can enable opportunities in this area. Ms. Grant briefed the Subcommittee on the development of workshop ideas and outreach to VCs. The Subcommittee proposed piloting a small workshop to convene senior-level NCI staff and the private sector, particularly the VCs that fund industry, to begin the dialogue. One aim is to ascertain why small companies are not interested in advancing their products that could eventually lead to profit and help patients. The Subcommittee discussed how helping people outside NCI to leverage its resources could align the incentives of the private sector, NCI, the FDA, and advocacy groups and could lead to better care for the cancer patient.

Questions and Answers

Dr. Hayes Dixon explained that the Subcommittee is interested in establishing a quarterly seminar or another forum to highlight PIs in the presence of industry representatives to better understand what is considered scientifically cutting-edge and identify what industry is interested in supporting that science. Dr. Rathmell noted the need to take every opportunity to break down the wall between government and industry, whether it is hosting a symposium or some other way of convening people to begin this dialogue.

Ms. Grant commented on the importance of building relationships and NCI's and NCAB's maintaining autonomy with regard to compliance and conflict of interest. The aim is to understand the right nexus to build relationships within NCI that are appropriate and within the confines of guidance, and also to allow the exceptional knowledge within NCI to permeate into the private sector where appropriate. This Subcommittee can serve as a nexus for investors who fund new therapies through startup companies and the investigators who help conduct clinical trials. Dr. Boxer added that the Subcommittee suggested hosting an open forum or roundtable and inviting a previous NCI director who has been in the private sector to teach investigators (intramural and extramural) how to bring their product or discovery to market. Ms. Grant highlighted Vanderbilt University's Center for Pharmaceutical Discovery, which has been an exceptional model of a public–private partnership, including compliance.

Dr. Azad noted that the NCAB Subcommittee on Clinical Investigations received feedback from a survey of the performance of the NCTN facilitated by Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program, DCTD, NCI. A common theme from the Cancer Centers was not being compensated to match industry to enroll participants on clinical trials, which creates major hurdles, especially in today's funding environment. Questions remain about whether NCI can leverage the more-than-20-year-old infrastructure of clinical trials through the NCTN in collaboration with VCs and new companies or whether it will require a reconfiguration.

Motion. A motion to accept the report of the 3 September 2024 NCAB *ad hoc* Subcommittee on Experimental Therapeutics e meeting was approved unanimously.

NCAB *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities.
Dr. Winkfield, Chair of the NCAB *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities, presented the report of the 3 September 2024 meeting. Dr. Winkfield reported that the Subcommittee reviewed the charge and heard a detailed overview of the Community Partnerships to Advance Science for Society (ComPASS) Program given by Dr. Cheryl Anne Boyce, Assistant Director for Re-engineering the Research Enterprise, Office of Strategic Coordination, The Common Fund, Division of Program Coordination, Planning, and Strategic Initiatives, Office of the Director, NIH. Dr. Boyce informed the Subcommittee that ComPASS, a Common Fund project, is leveraging partnerships across multiple sectors to develop and evaluate Community-led, Health Equity Structural Interventions (CHESIs) to reduce health disparities. The aim is to develop new health equity research

models for community-led and crosscutting structural intervention research across NIH and other federal agencies. ComPASS also will implement local Health Equity Research Assemblies, one of which NCI will lead. Dr. Winkfield noted that the Subcommittee looks forward to the outcomes of ComPASS and is considering ways to leverage this resource. The Subcommittee briefly discussed future topics and next steps; members will convene interim meetings to begin to review future partnerships and expertise to think about population health differently.

Questions and Answers

Dr. Rathmell asked about the best time to align with and leverage the efforts of ComPASS. Dr. Winkfield noted that the program is early in its work and that the infrastructure is still being built. She suggested identifying a cancer-related research question that could be addressed with this approach.

Motion. A motion to accept the report of the 3 September 2024 NCAB *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities meeting was approved unanimously.

New Business: Dr. Boxer noted the differences between the mandates of the BSA and NCAB and their activities. He highlighted the importance of meeting separately from the BSA to better focus on policy and to meet in person rather than virtually**.**

Dr. Gray explained that in prior years, during the months of February and March, in-person meetings were not held because of inclement weather during those months, especially in February. As such, the Boards had agreed to only meet in person during the months of June, September, and December. She also noted that the decision to continue having joint BSA/NCAB meetings resided with the NCI Director.

Dr. Rathmell agreed that in-person meetings are different from meeting virtually. As far as the Boards meeting jointly, consideration would be given to how to maximize the number of times the Boards meet and the fiscal responsibility that would be encountered if meetings are canceled, as well as the financial losses. As such, consideration would be given to the request and noted that there are other opportunities for in-person interactions, including attending workshops.

NCAB members indicated a preference of having separate/in-person meetings since concepts presented during the joint BSA/NCAB meetings limited the time for NCAB focused discussions.

Future Agenda Items. The NCAB members were asked to forward any further suggestions for potential future agenda items to Drs. Carpten and Gray.

XII. ADJOURNMENT OF OPEN SESSION—DR. JOHN D. CARPTEN

Dr. Carpten adjourned the open session. Only Board members and designated NCI staff remained for the closed session.

XIII. CLOSED SESSION—DR. JOHN D. CARPTEN

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., and section 1009(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. §§ 1001-1014).

There was a review of grants and a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent

The Board was informed that a comprehensive listing of all grant applications to be included in the **en bloc** vote was in the Special Actions package. Those grant applications, as well as those announced during the closed session, could be considered for funding by the Institute.

The NCAB **en bloc** motion to concur with IRG recommendations was unanimously approved. During the closed session, a total of 2,334 NCI applications were reviewed requesting direct cost support of $960,980,432.

XIV. ADJOURNMENT—DR. JOHN D. CARPTEN

Dr. Carpten thanked all the Board members, as well as the visitors and observers, for attending. There being no further business, the 168th regular meeting of the NCAB was adjourned at 4:10 p.m. on Wednesday, 4 September 2024.

Date — John D. Carpten, Ph.D., Chair, NCAB

Date — Paulette S. Gray, Ph.D., Executive Secretary