U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
19th VIRTUAL NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
6 September 2023

Virtual Meeting
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
6 September 2023

The National Cancer Advisory Board (NCAB) convened for its 19th virtual regular meeting on 6 September 2023. The meeting was open to the public on Wednesday, 6 September 2023, from 1:00 p.m. to 3:53 p.m. and closed to the public from 4:15 p.m. to 5:20 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 (absent)
Dr. Nilofer S. Azad
Dr. Anna D. Barker
Dr. Richard J. Boxer
Dr. Luis Alberto Diaz, Jr.
Ms. Ysabel Duron
Dr. Howard J. Fingert
Dr. Christopher R. Friese
Ms. Julie Papanek Grant* (absent)
Dr. Andrea A. Hayes Dixon
Dr. Amy B. Heimberger
Dr. Nikan Khatibi
Dr. Ana Navas-Acien
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

Alternate *Ex Officio* NCAB Members

Dr. John Gordon, CPSC
Dr. Joseph R. Graber, DOE
Dr. Michelle Heacock, NIEHS
(Alternate for Dr. Gwen W. Collman)
Dr. Michael Kelley, VA (absent)
Dr. Julie Schneider, FDA (Alternate for Dr. Richard Pazdur)
Dr. Tara A. Schwetz, NIH (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Monica M. Bertagnolli, Director, National Cancer Institute
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. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
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. Ed Harlow, Special Advisor to the NCI Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies McConville, Acting Director, Office of Scientific Operations, NCI at Frederick
Dr. Douglas R. Lowy, Principal Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Dr. Meg Mooney, Associate Director, Cancer Therapy Evaluation Program
Dr. Diane Palmieri, Acting Director, Center for Research Strategy
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
Ms. Donna Siegle, Executive Officer and Deputy Director for Management, Office of the Director
Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development
Dr. Sanya A. Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology Transfer Programs
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

TABLE OF CONTENTS

I. Call to Order and Opening Remarks—Dr. John D. Carpten 1
II. Future Board Meeting Dates—Dr. John D. Carpten 1
III. NCI Director's Report—Dr. Monica M. Bertagnolli 1
Questions and Answers 4
IV. Legislative Report—Ms. M.K. Holohan 5
Questions and Answers 6
V. Budget Overview—Mr. Weston Ricks and Dr. Douglas R. Lowy 6
Questions and Answers 8
VI. Collaborative Approaches to Accelerate Better Therapies for Patients With Rare Tumors—
Drs. Brigitte C. Widemann and Karlyne M. Reilly 9
Questions and Answers 13
VII. Ongoing and New Business—Dr. John D. Carpten 14
Future Agenda Items 14

VIII. Adjournment of Open Session—Dr. John D. Carpten 14
IX. Closed Session—Dr. John D. Carpten 14
X. Adjournment—Dr. John D. Carpten 15

WEDNESDAY, 6 SEPTEMBER 2023

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

Dr. John D. Carpten called to order the 19th virtual National Cancer Advisory Board (NCAB) meeting. He welcomed members of the Board, *ex officio* members, liaison representatives, President's Cancer Panel members, 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 14–15 June 2023 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. MONICA M. BERTAGNOLLI

Dr. Monica M. Bertagnolli, Director, NCI, welcomed NCAB members and attendees to the 19th virtual meeting and provided an update on NCI news, recent highlights including the National Cancer Plan, cancer research advances, and future activities.

NCI News. Dr. Bertagnolli remarked on the uncertainty of the amount of research that the NCI will be able to support in fiscal year (FY) 2024, given the budget concerns. She noted that today's agenda has been structured to address this situation. Congress is currently working on the FY 2024 budget agreement; the budget period begins on 1 October 2023. The NCI submitted its *Annual Plan and Budget Proposal for FY 2024* (also called the Bypass Budget), which is intended to inform the development of the President's Budget and the overall National Institutes of Health (NIH)/NCI appropriations process. This proposal, which the NCI produces because of its special budgetary authority, provides the optimum funding for FY 2024 to conduct rapid cancer research. In addition, it increases the budget as necessary to achieve NCI's ambitious goals. In March 2023, the President's FY 2024 budget was submitted to Congress and included a robust increase for the NCI. This budget release starts the appropriations process; Congress is determining the FY 2024 appropriations for the NCI and other agencies. Later in September 2023, the NCI will publish its FY 2025 Professional Judgment Budget, and it will align with the President's FY 2024 budget increases. Dr. Bertagnolli commented that these generous increases in NCI's budget are well justified by the incredible opportunities and significant progress the NCI and its investigators are poised to offer the American people.

In August 2023, the NCI announced the establishment of the NCI Worta McCaskill-Stevens Career Development Award for Community Oncology and Prevention Research. Dr. McCaskill-Stevens, who is Director of NCI Community Oncology Research Program (NCORP) and Chief, Community Oncology and Prevention Trials Research Group, Division of Cancer Prevention (DCP), has been a powerful leader for many years in implementing NCI's goal to bring cancer research to the communities where people live, particularly to those who experience cancer disparities. Throughout her career, She has 1) had a passion and commitment to follow the road less traveled, 2) changed the trajectory of community cancer research, and 3) inspired others to follow in her footsteps. Dr. Bertagnolli conveyed that to overcome the many challenges confronted in cancer research, the NCI needs to nurture more leaders like Dr. McCaskill-Stevens who embody this commitment. A notice of funding opportunity will be issued to support institutional career development programs designed to train clinical scientists in community

cancer prevention, intervention, and treatment research. This award will be widely available for such programs, and special emphasis has been placed on training clinical scientists whose career goal is to meet the needs of underserved or marginalized communities to increase their access to clinical care and participation in research.

Momentum Toward Achieving the Goals of the Cancer Moonshot℠ and National Cancer Plan. The NCI continues to build momentum for the National Cancer Plan (NCP, the Plan), which not only benefits the NCI but everyone in the cancer community. The Plan focuses all efforts on achieving the President's Cancer Moonshot goals to reduce the age-adjusted cancer mortality rate by 50 percent by 2047 (i.e., in 25 years) and to transform cancer into a livable, treatable disease for all people. On 7 September 2023, the President's Cancer Panel (PCP), i.e., the Chair, Dr. Elizabeth M. Jaffee (Sidney Kimmel Comprehensive Cancer Center, Skip Viragh Pancreatic Cancer Center, and Johns Hopkins University), Dr. Mitchell Berger (University of California, San Francisco), and Dr. Carol L. Brown (Memorial Sloan Kettering Cancer Center), will convene the initial NCP stakeholders meeting. Representatives from the nation's largest cancer-related organizations will attend, and each will share the actions being taken to address the goals of the NCP. The meeting is virtual and open to the public, and 250 people have registered. The response to the NCP has been tremendous, and the NCI appreciates the leadership of the PCP in this critical engagement. The University of Colorado Cancer Center is one of the first research groups to announce its actions and has posted a series of stories on its website about how it is working toward each of the Plan's eight goals.

In mid-September 2023, the White House will convene the Cancer Moonshot Cancer Cabinet to continue the common goals and coordinate across federal agencies. This Cabinet represents the President's all-of-government approach to "ending cancer as we know it." A fact sheet with highlights from the meeting will be made available to the public.

The U.S. Department of Health and Human Services (HHS) will soon launch a cancer data initiative, a Cancer Moonshot collaboration that is aligned with the NCP goals to maximize data utility. The Office of the Secretary of the HHS is coordinating this initiative, which is being led by multiple health-focused agencies, including the NCI, Centers for Disease Control and Prevention (CDC), NIH, U.S. Food and Drug Administration (FDA), Advanced Research Projects Agency for Health (ARPA-H), and Office of the National Coordinator for Health Information Technology (ONC). This effort is in the planning stages and will coordinate across the HHS. Activities will include developing a standard schema for data linkages across the HHS; creating data standards and interoperability; and building partnerships between the public and the private sectors to power the adoption of data sharing across U.S. health agencies and health systems. Dr. Bertagnolli noted that the existing resources are numerous but are not optimized to take full advantage of their potential to reveal insights that will prevent cancer. A collaboration at a massive scale to leverage and connect the respective strengths and resources is needed. The NCI expects that this HHS-wide initiative will be a step in that direction and also provide a road map for improving all health, not just preventing cancer.

Implementing the NCP's Goals. Dr. Bertagnolli highlighted recent progress of the NCP across the eight goals, all of which required collaboration for success. In terms of prevention, screening, and early detection, the NCI recognizes that it is critical to find ways to stop cancers before they develop, or, alternatively, have the ability to detect cancers early to successfully treat them. In 2021, the NCI announced the national Vanguard Study to evaluate whether multi-cancer detection (MCD) can identify cancers early to reduce deaths and determine whether the benefits of these tests can outweigh the harms. Trial enrollment is expected to begin in 2024. Dr. Bertagnolli explained that the ability to screen for many cancers at once through a simple blood draw could have a profound effect on outcomes, and these tests could also potentially boost uptake of cancer screening if MCD tests are included in routine visits to primary care physicians. No trials exist that show whether MCD tests reduce cancer deaths or whether the

downstream effects on health care services and potential for overtreatment are addressed. The NCI recognizes the real concerns that the Vanguard Study will address: critical questions about cancer screening, including efficacy, adoption, and implementation. In addition, the NCI has a robust portfolio of work (e.g., the NCI Cervical Cancer 'Last Mile' Initiative) to address these NCP goals.

To advance clinical trials, the NCI is working to transform trials so that they achieve results faster and better serve everyone. Two key challenges being addressed are increasing trial accruals, particularly of underrepresented populations, and streamlining trials to be cost-effective and deliver results more efficiently. The intent is to move away from routine practices that no longer serve the needs of the cancer community and to test new models that can transform clinical trials. The NCI recently established the Clinical Trials Innovation Unit (CTIU) and activated the innovative Pragmatica–Lung cancer treatment trial and Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice (ComboMATCH) trials.

Regarding health disparities research, a priority for the NCI has been to close gaps that lead to higher incidence and mortality for some populations, particularly those who have long been confronted with systemic barriers to research and health care. The NCI has launched several new programs over the last few years, including the Persistent Poverty Initiative (PPI), Connecting Underrepresented Populations to Clinical Trials (CUSP2CT), and Telehealth Research Centers of Excellence (TRACE), to advance disparities research into new areas to better understand these gaps.

In the area of workforce training, NCI's commitment to advancing the future of cancer research through its investments in people and essential infrastructure makes possible most of the progress that cancer patients need. The NCI provides critical opportunities to strengthen the workforce by bringing the widest possible variety of ideas and perspectives to deliver the best cancer science. This includes newer programs to fund and mentor scientists from diverse backgrounds, which helps to build the pipeline of talented cancer researchers that is desperately needed to meet today's opportunities. Dr. Bertagnolli underscored that diversity among scientists is vital to asking the right research questions and understanding the challenges that are faced by all populations. One such NCI program is the Cancer Moonshot Scholars, which has the goal of advancing science through greater diversity in the NCI R01 applicant pool. R01 grants are the source of many innovative ideas and some of the most significant discoveries in cancer research. The NCI recently announced the first Cancer Moonshot Scholars cohort of 10 investigators, whose research projects extend across cancer sites and scientific disciplines from basic science to treatment to implementation science.

For data sharing and infrastructure, the NCI has made essential investments in cancer data and technology that are transforming what is possible for cancer research. Efforts include building infrastructure that connects vast collections of data to power more robust analysis and creating three-dimensional tumor atlases that are making it possible to detect how cancer evolves from precancerous lesions to advanced disease. Dr. Bertagnolli remarked that these resources are only as good as the quality and quantity of the data and that investments in collecting sufficient data from all populations to know what works for each is critical. To collect such data, it is absolutely essential that people with cancer or at risk of being diagnosed with the disease have the opportunity to contribute their information. The NCI, therefore, focuses on several data collection activities, providing the potential to learn from every patient and improve results for everyone. Examples include the National Cancer Data Ecosystem, Cancer Research Data Commons (CRDC), Clinical Proteomic Tumor Analysis Consortium (CPTAC), and Human Tumor Atlas Network (HTAN). Dr. Bertagnolli highlighted that the Childhood Cancer Data Initiative (CCDI) has made tremendous progress in the few years since its launch to make data accessible that historically have been very challenging for researchers to access. Childhood cancers can be rare, and these data often are stored in hospitals where it can be hard to access. The CCDI helps researchers study these rare cancers and will help oncologists and their patients make the best possible treatment decisions.

The CCDI recently facilitated the release of new data sources, including the Children's Brain Tumor Network, Pacific Pediatric Neuro-Oncology Consortium, and Children's Hospital of Philadelphia Division of Genomic Diagnostics. Launched as a data sharing initiative, the CCDI has now become a community focus for research directed at overcoming pediatric cancers.

FY 2023 Cancer Research Advances. Dr. Bertagnolli reported on recent cancer research progress among the intramural and extramural research programs across the cancer research continuum. In the area of basic science, the cancer field better understands what drives the growth of pancreatic cancer, how colorectal cancer metastasizes, and what can promote the formation and progression of esophageal cancer. In addition, a number of the basic science studies could potentially benefit those who are working to prevent and treat cancer. For implementation science, NCI investigators, via Cancer Moonshot–funded programs, revealed that clinician-focused nudges using electronic health records can result in more cancer patients engaging in tobacco-use treatment. Research focused on cancer survivors provides a better understanding of the association of metabolic syndrome in cancer survivors by gender. This same study also found that men with a history of hematologic malignancies and women with cervical cancer were at the greatest risk of developing metabolic syndrome.

An NCI clinical trial investigating advanced alveolar soft part sarcoma (ASPS) led to the first FDA approval of atezolizumab to treat adults and children 2 years and older with this rare cancer. Dr. Bertagnolli highlighted this trial as one example of accomplishing the goal of "ending cancer as we know it" for all people. She emphasized that research funded by the American people can focus on rare cancers, which are understudied within the cancer research community overall for a variety of reasons. This ASPS trial was conducted at the NIH Clinical Center, which makes it possible to bring in patients from all parts of the world for dedicated studies on rare cancers and is the only way to make progress quickly.

NCI's Future Activities. Dr. Bertagnolli explained that the NCI has two primary components in place that are poised to address the big scientific challenges of this field: sustaining current and new programs (e.g., Clinical Trials Innovation Unit (CTIU), Persistent Poverty Initiative (PPI), Childhood Cancer Data Initiative (CCDI)) and increasing the Research Project Grant (RPG) paylines. The NCI also is committed to promoting more comprehensive systems biology work; expanding community outreach and engagement work through the NCI-Designated Cancer Centers (Cancer Centers), with a focus on underserved populations; fostering direct patient engagement; expanding the prevention and screening network; and enabling more clinical trials. Furthermore, the NCI will leverage the data ecosystem and data to power machine learning, foster new collaborations within ARPA-H, and enhance support for cancer research trainees.

In closing, Dr. Bertagnolli underscored that the NCI is committed to doing everything to power cancer research across the full spectrum, from basic discovery of cancer biology to understanding how to deliver the very best health care for all who need it. However, there remains much to do to accomplish the ultimate goal of combating this terrible disease. Expanding on the many recent successes will require action at all levels of society. The starting point of this action is research, which is the primary objective of the NCI.

Questions and Answers

NCAB Chair Dr. Carpten asked for examples or insight on how the Cancer Cabinet is working with the NCI and NIH and how those efforts are advancing the Cancer Moonshot. Dr. Bertagnolli reiterated that the HHS-wide data integration is one such example and for the first time will enable cancer data that are collected by the Center for Disease Control and Prevention (CDC), Centers for Medicare and Medicaid Services (CMS), FDA, and NIH to be centralized. The Office of the National Coordinator for Health Information Technology (ONC) is a partner in this effort and will make common data

comparisons, doing so at scale. This initiative will be presented during the next Cancer Cabinet meeting and will highlight what one agency (the HHS) can do. Other cross-agency collaborations include the Department of Defense (DoD), Environmental Protection Agency (EPA), and Federal Emergency Management Agency (FEMA).

Dr. Ana Navas-Acien, Professor of Environmental Health Sciences, Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, suggested including cancer-related environmental data from the EPA and U.S. Geological Survey in the HHS-wide data initiative. Dr. Bertagnolli noted that the first priority is to collect data on what is happening to people in the clinical care environment. She added that HHS data streams (e.g., CMS, CDC) seem to be the appropriate places to begin. She anticipates that data from efforts related to the ARPA-H collaborations will bring together a federated data environment that will allow data from other sources, including the EPA and potentially the Department of Veterans Affairs (VA). She explained that the clinical care environment has the mandate to develop a process or procedure so that every individual patient who has given permission to use their data knows where these data are being utilized, which is not an easy task.

Dr. Anna D. Barker, Chief Strategy Officer, Ellison Institute for Transformative Medicine, University of Southern California, inquired about the ARPA-H collaborations and the intersection with industry. Dr. Bertagnolli explained that the NCI views this collaboration as a partnership and noted that ARPA-H's research model of focusing on solving critical problems complements NCI's model, which is to take the long view, from molecular discovery to what happens in a patient. This approach can significantly help the NCI with its longitudinal plans for ongoing and new programs. ARPA-H soon will announce an NCI data collaboration opportunity. The NCI intersects the private for-profit community in many ways through the Small Business Innovation Research program, which is bridging the gap by advancing new technologies and therapeutics to commercialization, and the NCI National Clinical Trials Network (NCTN), which is creating a system where drugs, devices, and other needed resources are obtained for conducting research.

Ms. Ysabel Duron, Founder and Executive Director, The Latino Cancer Institute, asked whether the NCI will either integrate or intervene to ensure that the public understands and does not fear the convergence of artificial intelligence (AI) with science. Dr. Bertagnolli commented that AI and machine learning are new ways of analyzing data that can produce insights that are not immediately obvious and can command large data collections to do so. She noted the need to be effective communicators to the public to convey why these new techniques are being used in the research community and the potential for positive impact on new treatments in the clinic. She also noted the need for the public to understand that the NCI conducts research with people and engages people in a manner of trust and bidirectional communication.

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

Ms. M.K. Holohan, Director, Office of Government and Congressional Relations, NCI, reported on the debt limit budget deal, FY 2024 appropriations, and congressional work ahead. In June 2023, the President signed into law the Fiscal Responsibility Act of 2023 (FRA) to raise the U.S. debt limit, with spending caps that will result in a "lean" FY 2024 budget. Key provisions in the FRA suspend the debt ceiling for 2 years (until 1 January 2025) and cap government spending at the FY 2023 level. Specifically, the agreement rescinds $20 billion (B) in Internal Revenue Service funding allocated through the Inflation Reduction Act of 2022 and has a penalty attached that will impose a 1% cut across all government spending (notably, including Defense) for FY 2024 by 1 percent if Congress fails to pass all 12

appropriations bills by January 1, 2024 (this reduction becomes permanent if the bills are not done by April 30, 2024).

Ms. Holohan explained that the NCI receives its funding from Congress as part of the overall federal budget process. Relatedly, the NCI also develops an annual Professional Judgment Budget (previously described by Dr. Bertagnolli), authorized by the National Cancer Act of 1971, and is the only NIH institute that has this authority for its full operating budget. An NIH Professional Judgment Budget for Alzheimer's Disease and Related Dementias, in accordance with the Consolidated and Further Continuing Appropriations Act, 2015, is authored by the National Institute of Aging on behalf of the NIH.

The Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS), is writing its spending bills to FRA levels, with an additional $23B in emergency funding ($2B for Labor-HHS). However, after a small group of House Republicans revolted against the FRA deal that Speaker Kevin McCarthy brokered with Democrats and the White House, the House GOP adopted a view that the FRA level of FY23 funding was "the ceiling, not the floor" and proceeded to write its FY 2024 spending bills to the lower FY 2022 levels, which amounts to at least $119B less than the FRA level, and does not include emergency funding, creating a wide chasm with the Senate.

The House and Senate have major differences not only in the topline budget numbers they want, but also in how they believe lawmakers should fund federal agencies in the short and long term, from supporting supplemental funding measures to on-time funding to no support for a continuing resolution (CR) with the inclusion of a border security bill. A CR is a stopgap funding measure to continue government funding while the two parties negotiate their differences. Ms. Holohan noted that Senator Patty Murray (D-Washington), Chair of the Senate Appropriations Committee, and Senator Susan Collins (R-Maine), Ranking Member, have been colleagues for decades and have a reputation for valuing a bipartisan process and bipartisan engagement in negotiations. These leaders are determined to implement a bipartisan process in the Senate Appropriations Committee and have unanimously passed their bills out of committee.

The House and Senate appropriations subcommittees Labor-HHS bills also take different approaches to NIH and NCI funding. The House declined to continue the $216 million (M) appropriation for the FY 2023 Cancer Moonshot. The past 7 years included mandatory funding via the 21st Century Cures Act, with decreasing funding levels over time. The appropriators have backfilled those numbers, but those do not reflect an absence of Cancer Moonshot funding in a flat budget environment. The Senate would continue that funding but would also provide an increase of $60M. The negotiation process for both chambers will be challenging. CRs have been very common over the past years and sometimes extend for an entire fiscal year. Ms. Holohan noted that the NCI is cautiously optimistic that a short duration CR (less than 1 year) will be agreed upon to fund the government.

Questions and Answers

Questions and answers were deferred to the budget overview discussion.

V. BUDGET OVERVIEW—MR. WESTON RICKS AND DR. DOUGLAS R. LOWY

Mr. Weston Ricks, Director, Office of Budget and Finance, NCI, reviewed the budget landscape in the context of NCI activities. Mr. Ricks explained that while the NCI budget has increased over the past 20 years in nominal terms, the NCI's research buying power lags behind the purchase power it had in 2023. Contributing to this gap is that the NCI portfolio has become more complicated in its support of 10 additional Cancer Centers, numerous new programs and grant mechanisms, and several new initiatives.

Cumulatively, across the past 20 years, the total missed research opportunities due to inflation alone amount to an estimated $21 B.

NCI's annual fiscal year budgetary costs comprise three major areas: out-year commitments to continuing activities (e.g., grants, clinical trials, and Cancer Centers); operating costs and assessments, which include program evaluations, technology for reporting and transparency, and cybersecurity efforts; and new scientific opportunities, such as the Cancer Moonshot. Mr. Ricks further elaborated on the out-year commitments, focusing on NCI grant commitments over time. The grants portfolio comprises $4.4B of the overall annual budget that supports ongoing and new awards. The following year and beyond, the NCI will support a more costly set of new or recompeting grants, and each new set builds on the previous years' work. Because of inflation and new technologies, each grant costs more to sponsor and implement. At the same time, the NCI is supporting the out-year costs for its 5-year grants, which is a significant commitment. In terms of the potential widening gap in the funding out-years, Mr. Ricks emphasized that the NCI has 13 percent less buying power in 2023 than in 2003, which presents a significant gap in research that can be supported. He noted that according to Ms. Holohan's report, a CR is likely, suggesting no changes in the annual budget. The NCI projects $276M increase to FY 2024 costs attributed to inflation and that amount will be needed to minimally sustain NCI programs.

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, provided an overview of the RPG pool budget and other critical components of cancer research through funding mechanisms outside the RPGs. He also discussed the possible impact of the proposed FY 2024 budget on NCI activities. The goal of the NCI budget and programs is to improve health outcomes. Critical components of the interconnectedness of the NCI budget and programs include research funding, training and workforce development, resources for researchers, operating expenses, the Cancer Centers, and clinical trials. The RPG pool is the largest investment of NCI funding, at 44 percent of the total budget in FY 2022. From FY 2013 to FY 2022, both the rate of applications and number of applicants to the NCI increased substantially more than for other NIH institutes and centers. This increase ultimately will be reflected in a decrease in paylines and funding success rates. From FY 2018 to FY 2022, the RPG pool budget increased from 41 percent to 44 percent, representing an average of $140M annually, and it is anticipated to increase further in FY 2023.

From FY 2016 to FY 2022, 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. During this same period, the NCI increased paylines for early stage investigators (ESIs) R01/R37 by 5 percent, resulting in an increase from the 12th to 17th percentile. The NCI is funding noncompeting RPG awards at less than 100 percent of the commitment level. The NCI considers this option only when funds from the turnover of completed awards plus funds from NCI appropriation are insufficient. In these situations, the overall issue is whether to prioritize making more awards (i.e., having a higher payline) or to prioritize funding noncompeting grants at 100 percent. The NCI typically prioritizes funding additional competing awards.

From FY 2012 to FY 2022, the number of NCI modular awards (up to $250K in direct costs) progressively decreased from 63 percent to 17 percent. The NCI decreased the budgets of these awards by 8.5 percent, amounting to $225K in direct costs. During this same period, the number of NCI non-modular awards (greater than $250K in direct costs) increased from 39 percent to 80 percent, with an average direct cost of $425K per grant. Dr. Lowy noted that this change in non-modular awards is a tangible reflection of the impact of inflation and that the NCI projects that this trend will continue to increase to 90 percent or higher over the next 2 to 3 years. The NCI funds many critical components of cancer research through mechanisms outside the RPGs, including Specialized Programs of Research Excellence (SPOREs), Cancer Center Support Grants (CCSGs), cancer training, and clinical trials networks.

Dr. Lowy discussed the implication of a "flat" budget. Because the Cancer Moonshot funds were never part of the NCI base budget, the House budget marked for FY 2024 did not consider that the $216M for this funding would decrease to zero in FY 2024. In contrast, the Senate's marked-up bill did consider that this funding would end and added the $216M to the base budget, plus an additional $60M. To maintain the 12th percentile payline, the NCI will need to add $250M to the RPG pool to fund new awards, as well as to fund noncompeting awards at 100 percent. The NCI incurs between $75M and $100M annually in increased mandatory expenses (e.g., program evaluations, cybersecurity, Center for Scientific Review (CSR) expenses). All components of the NCI budget could adversely be affected by a flat budget. The NCI would be confronted with decreasing the payline for new RPG awards and funding noncompeting awards at less than 100 percent. Decreases that were not previously considered will need to be contemplated for the competing renewals of CCSGs and cancer training awards, as well as for the noncompeting CCSGs. The cuts to the intramural research program are anticipated to be along the levels of the extramural awards.

Dr. Lowy noted that the FY 2024 budget is not likely to be as favorable as previous budgets. The NCI is actively focusing on prioritizing and supporting the most critical cancer research and will continue to make the best progress possible in cancer research.

Questions and Answers

In response to a question from Dr. Barker about opportunities in the election year to move the budget environment in a different direction, Ms. Holohan explained that although budget caps are in place, not all agencies or programs will be funded at the same levels. The House and Senate are selecting different areas of cancer research to support, but she does not expect granularity at the IC level. Issues likely to affect the Presidential election are a potential government shutdown in FY 2023; the creation of a more dangerous situation in Ukraine because of changing support; COVID aid rescissions of unspent money; and AI and competitiveness with China. Dr. Bertagnolli commented that the HHS data initiative is not receiving additional funding and will be supported by existing funds as a priority across participating agencies.

Dr. Andrea Hayes Dixon, Dean, Howard University College of Medicine, Vice President of Clinical Affairs, Chair of Surgery, Howard University Hospital, asked whether funding to the Cancer Centers would be decreased based on established metrics. Dr. Lowy explained that the NCI is actively discussing what the impact of the FY 2024 budget would be on the CCSGs, which have had steady increases with each grant renewal. Dr. Bertagnolli added that the NCI is focusing on priorities and how to best support the entire community. Small cuts across all programs or large cuts to a specific program are approaches that the NCI is considering. The NCI also is evaluating consolidating processes, identifying economies of scale, seeking ways to eliminate redundancies, and graduating mature projects, all aiming to reduce costs. Cancer Center funding is leveraged multiple times across centers and generates a significant return on investment.

In response to a question from NCAB Chair Dr. Carpten about the impact of the budget on the NCI at Frederick, Dr. Bertagnolli commented that all segments of the NCI will be affected, including the NCI at Frederick and the Frederick National Laboratory for Cancer Research (FNLCR). As a Federally Funded Research and Development Center (FFRDC), FNLCR serves as a supportive institution that has multiple areas of intersection with NCI programs. FNLCR manages core laboratory resources used by the extramural community, such as the National Cryo-Electron Microscopy Facility (NCEF); manages contracting services used by the NCTN; provides a contracting authority for those services; and participates in ARPA-H activities. The NCI is reviewing these complex interrelationships to inform decisions on the most efficient use of the NCI budget.

From the perspective of advocates around the country, Ms. Duron asked whether the NCI has metrics for evaluating which of the comprehensive Cancer Centers are, in fact, addressing and achieving health disparities goals and then factoring that into the budget decisions. She also asked about plans for incentives for those centers providing more community outreach in communities of color, for example. Dr. Lowy noted that health disparities research still seems to be underfunded and under researched, regardless of the investments, but this research also may be affected by the budget situation. He also noted the many factors by which Cancer Centers are judged, including the peer-review process. Dr. Bertagnolli added that the NCI Center to Reduce Cancer Health Disparities (CRCHD), which addresses workforce diversity in detail, is responsible for such evaluations and is involved in many support mechanisms to extend health disparities research, some of which are implemented directly through the Cancer Centers and others that are independent researcher-initiated awards.

Dr. Amy B. Heimberger, Jean Malnati Miller Professor of Brain Tumor Research, Vice Chair for Research, Department of Neurosurgery, Northwestern University Feinberg School of Medicine, suggested developing key performance metrics (e.g., enhancing diversity, training, or catchment areas) for Cancer Centers to streamline the NCI renewal process for the directors and moving away from convening internal and external advisory boards to inform centers' programs, which may be distractions. Dr. Bertagnolli agreed with reducing routine activities that do not produce value. As a previous member of Cancer Center advisory boards and a recipient of their interactions and advice, she emphasized the value in having these boards to help establish relationships, network, eliminate silos, and establish joint programs. NCAB Chair Dr. Carpten suggested that this be a topic of discussion at a future meeting.

NCAB Chair Dr. Carpten asked how the budget situation affects the Cancer Moonshot activities. Dr. Dinah S. Singer, Deputy Director, Scientific Strategy & Development, noted that the NCI has been planning how to maintain and continue to support the critical research that was started under the Cancer Moonshot. A number of programs have been completed, and others have transitioned to RPG funding. The NCI has set aside funding to support the existing programs until they can transition to RPG funding over the next 1 to 2 years. Dr. Singer offered to provide an update on this topic at a future meeting.

VI. COLLABORATIVE APPROACHES TO ACCELERATE BETTER THERAPIES FOR PATIENTS WITH RARE TUMORS—DRS. BRIGITTE C. WIDEMANN AND KARLYNE M. REILLY

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, reported on the landscape analysis of rare-tumor research and provided an update of NCI's rare tumor research efforts. Rare tumors are defined by the NCI as an incidence of less than 150 cases per 1 million persons per year. Twenty-seven percent of new cancer diagnoses fit this category, and 25 percent of cancer deaths can be attributed to rare cancers. All pediatric cancers, central nervous system cancers, and sarcomas are rare. Patients with rare cancers experience numerous challenges, including the long length of time to diagnosis, limited expertise at many medical centers, lack of a standard of care, and limited social and advocacy support. Challenges for researchers investigating rare cancers are the long time accruing patients to clinical trials, limited tools and diversity of models, inadequate support from granting agencies, and minimal financial incentives for industry to collaborate on drug development. The NCI has been working to address these challenges for both patients and researchers.

In 2019, when the CCDI launched, the NCI observed that many rare-tumor efforts were ongoing, but these efforts were not well-connected as a network. A landscape analysis of the scientific literature and an internet search for rare-tumor research programs identified 76 such programs. A survey of 42 of the 76 programs was conducted from May to November 2021, and 23 groups responded. The results

revealed that the primary sources of funding were philanthropy, advocacy, and government. Data collected include clinical, biospecimen, family history, and patient-reported outcomes (PRO). Only a few programs collected longitudinal data. Many of the programs share their data in NIH databases. Some of the survey responders commented on the difficulty of finding and sharing data and making it accessible, which is an issue Dr. Widemann noted that the CCDI is aiming to address.

My Pediatric and Adult Rare Tumor Network (MyPART). MyPART is a Cancer Moonshot–supported project that aims to increase patient and family involvement in rare-tumor research. The goal is to develop new therapies for rare pediatric and adult solid tumors through increased understanding of tumor biology and natural history. Efforts are (1) focusing on rare solid tumors affecting children, teens, and young adults (less than 39 years of age); (2) engaging patients, family members, advocates, clinicians, and scientists as partners in research; and (3) collecting longitudinal molecular, clinical, and PRO data through the Natural History and Biospecimen Acquisition for Children and Adults With Rare Solid Tumors (or Natural History Study of Rare Solid Tumors). The NCI, in collaboration with external partners, plans to host workshops and symposia on rare tumors to develop expert consensus and multiday clinics for rare tumors to bring patients and nationwide experts together at the NIH Clinical Center. The outcome will be the establishment of a multi-institutional network of sites to collaborate on data collection. Key accomplishments of MyPART include developing a natural history study with tumor-specific subprotocols; transitioning to remote enrollment during the COVID-19 pandemic; analyzing tumor and blood and saliva biospecimens; expanding the Rare Tumor Specialty Clinics at the NIH; and participating and contributing to interventional trials for children and adults with rare tumors in collaboration with the NCI Developmental Therapeutics Clinic (DTC). In addition, clinical and biospecimen data were submitted to the database of Genotypes and Phenotypes (dbGAP) and are expected to be publicly available by the end of 2023.

Dr. Widemann further elaborated on the Natural History Study of Rare Solid Tumors. This study is a standardized longitudinal investigation (retrospective and prospective) that collects medical and family history, PRO, and clinical evaluation. Extensive medical record data are obtained on children and adults with rare solid tumors and their biological relatives. Once enrolled, comprehensive molecular profiling is performed, biological samples are collected, and genetic counseling is provided as needed. Since January 2019, the study has enrolled a cohort of 571 patients from 46 states, including Washington, D.C., and Puerto Rico, and 27 countries outside of the United States. Predominate tumor types among the cohort include chordoma, wild-type gastrointestinal stroma tumor (GIST), neuroendocrine, adrenocortical carcinoma, and medullary thyroid carcinoma. In the early phase of the study, the majority of patients were enrolled at the NIH Clinical Center, which switched to virtual enrollment during the COVID-19 pandemic and also benefited volunteers residing in rural areas. To date, more females than males are enrolled in the study, primarily because of the predominance of the tumor types presented. Seventy-one percent of participants are White/Caucasian, and smaller percentages are of minority groups. A peer diversity working group and NCI's Center for Cancer Research (CCR) are working to increase recruitment in underrepresented populations in this study.

To collect PRO data, MyPART uses 25 instruments. Preliminary analysis demonstrates differences in PROs for particular tumor types and has led to expanded tumor-specific PRO collection in subprotocols. Molecular analysis of biospecimens using Trusight Oncology 500 Gene Panel sequencing has identified expected pathogenic mutations, and the proportion of pathogenic and actionable mutations varied by tumor. Using the wild-type GIST clinic model of convening patients, the NCI brings 10 to 15 patients with select very rare tumors to the NIH Clinical Center for a rare-tumor clinic. Patients meet with clinicians from across the country who have expertise with these diseases, and they also have the opportunity to meet one another and receive recommendations from the experts. In 2019, the NCI hosted the inaugural chordoma clinic and has since conducted clinics in medullary thyroid carcinoma. A clinic for adrenocortical carcinoma is planned.

Dr. Widemann described how the chordoma approach might be a paradigm for addressing very rare-tumor research. Chordomas are very rare sarcomas, affecting fewer than 300 patients per year; pediatric chordomas affect fewer than 30 patients annually. Deficiency in the tumor suppressor genes *SMARC B1* or *SMARCA4* have been linked to pediatric chordomas. In this approach, the NCI first established an internal CCR–Division of Cancer Epidemiology and Genetics (DCEG) chordoma working group; convened a national workshop, inviting leading researchers in the field; formalized a partnership with the Chordoma Foundation through MyPART; developed a natural history study of chordoma subprotocol; hosted the first pediatric chordoma clinic at the NIH Clinical Center; and established multi-institution virtual tumor boards. In 2020, a Pediatric Chordoma Working Group was established and is composed of 45 extramural members. The final step is to promote grant applications and new treatment trials for chordoma patients. Dr. Karlyne M. Reilly, Senior Associate Scientist, POB, NCI, and Dr. Sanjay Malhotra, Oregon Health & Sciences University, are co-principal investigators on a DoD grant to study SMARCB-deficient tumors. Dr. Widemann noted that this chordoma effort has translated into a collaboration with the NCI Cancer Therapy Evaluation Program and the Children's Oncology Group (COG) Pediatric Early Phase Clinical Trial Network (PEP-CTN). The MyPART team and DTC investigators have developed a multisite trial to evaluate two checkpoint inhibitors (tiragolumab and atezolizumab) in *SMARCB1*-deficient tumors. Patients can be enrolled in one of six different cohorts and are not limited by age. This trial is ongoing.

MyPART also made preclinical progress since the inception of the program. The MyPART team and colleagues developed new orthotopic patient–derived xenografts and organoid models of rare tumors from patient biopsies and generated genetically engineered mouse models of wild-type GIST (*Sdhb*-knockout and $BRaf^{V600E}$). MyPART maintains multiple communication platforms for outreach, including an informational website with support resources for patients and the *MyPART Minute* newsletter. The advocacy network consists of 29 partners.

Dr. Widemann noted lessons learned from MyPART. Advocacy and both clinical and scientific rare-tumor expertise are critical. NIH Rare Tumor Clinics provide insight not achievable through evaluation of single patients at multiple sites. Building meaningful cohorts is resource and time intensive. Focus on select tumor types is needed to accrue sufficient patient numbers. Partnerships with consortia, COG, community hospitals, advocacy groups, and national experts will be critical to accelerating progress in rare-tumor research. MyPART is developing a collaborative national strategy for very rare pediatric and adolescent and young adult (AYA) cancers, to be coordinated by the CCDI. The goal is to efficiently study and characterize rare tumors and advance therapies

CCDI and the National Rare-Tumor Effort. Dr. Widemann updated the NCAB on the CCDI Molecular Characterization Initiative (MCI) and a national rare-tumor initiative. MCI is a partnership between the NCI and COG Project:EveryChild that provides state-of-the-art molecular characterization at diagnosis. Results are returned to participants and treating physicians within 21 days. In its first year, MCI enrolled more than 1,000 participants from 47 states, as well as Canada, Australia, and New Zealand. As of August 2023, 3,057 participants have been enrolled.

In the CCDI-coordinated Rare Pediatric/AYA Cancer study, patients are enrolled via Project:EveryChild or are self-referred and receive either clinical or molecular characterization through the MCI research grade sequence in collaboration with the disease experts. Patients are monitored and followed longitudinally, and all data are deposited into the CCDI data ecosystem. The aim is that preexisting programs could participate in this NCI-coordinated effort (from a correct and timely diagnosis to longitudinal follow-up) as disease champions locally and internationally.

Proposal for a Public–Private Partnership (PPP) to Develop Drugs for Ultra-Rare Cancers. Dr. Reilly described a public–private partnership to enable drug development for ultra-rare tumors. The

NCI began discussions on this project in winter 2022, and the Foundation for NIH (FNIH), in partnership with the NCI, National Center for Advancing Translational Sciences, and FDA, planned stakeholder engagement. On 24 August 2023, FNIH, the NCI, and the FDA held a public virtual meeting "Creating a Public–Private Partnership to Support Development of Anti-Cancer Therapies for Ultra-Rare Tumor Indications" to solicit feedback from the community on the proposal, and this meeting was well attended by interested parties from industry, academia, and advocacy groups. No consensus on a definition of ultra-rare tumors currently exists, and Dr. Reilly noted sources of information to build upon. In 2021, the Connective Tissue Oncology Society (CTOS) published a working group report that defines ultra-rare sarcomas as those with an annual incidence of less than 1 in 1 million. The European Orphanet ranks rare diseases according to six prevalence categories, with the rarest being less than 1 in 1 million. These incidence data (1 in 1 million) correlate to approximately 340 new cases annually in the current U.S. population. Dr. Reilly compiled data from Orphanet and CTOS, and this analysis identified 222 ultra-rare tumors, 60 of which have characteristic molecular alterations. These data suggest that an estimated 75,000 people in the United States are affected by ultra-rare tumors annually, but this is partly based on European data. Further research is needed to provide more accurate values representative of the U.S. population. As of 1 September 2023, approximately 43 percent of participants in the MyPART study have an ultra-rare-tumor diagnosis.

Dr. Reilly highlighted guiding principles and assumptions for ultra-rare tumors that frame the basis for this proposed PPP. Patients with ultra-rare tumors are as deserving of curative therapies as patients with common cancers. Due to the high cost of drug development and very limited commercial market, drugs are unlikely to be economically sustainable under current supply-demand paradigms. Many of the critical steps of drug discovery and development fall to advocacy organizations and academic researchers. Existing potentially effective drugs may be shelved or otherwise unavailable due to lack of use in more common cancers and lack of economic incentive to continue development. Drivers of ultra-rare tumors exist, but they have not been exploited fully because they are specific to ultra-rare tumors. Dr. Reilly emphasized that the NIH and FDA are well poised to reduce hurdles in drug development for ultra-rare tumors by establishing PPPs to incentivize drug development and clinical trials, with the aid of the FNIH.

The aim of the PPP is to harness state-of-the art technologies to target well-established but previously undruggable biologic vulnerabilities of ultra-rare cancers that lack commercial incentives for drug development through open science, multi-stakeholder public/private partnership. The objectives are fourfold: 1) explore in depth the pathognomonic biology of select ultra-rare cancers to identify and characterize molecular vulnerabilities that confer potential druggable targets; 2) evaluate the feasibility and expediency of various drug development platforms to target the identified aberrant biology; 3) develop an open-science process across government, academia, and industry to leverage and coordinate resources in developing drugs for ultra-rare cancer indications; and 4) coordinate and champion the development, from concept to clinical trial, of a drug targeting the aberrant biology of an ultra-rare cancer.

The FNIH will provide governance and oversight for the PPP and will facilitate interactions between the government and other stakeholders. Dr. Reilly noted that the FNIH was established by Congress to help form bridges between the NIH and other entities and help provide fundraising, governance, intellectual property (IP) management, and many other functions needed for success. The NCI envisions an iterative cycle of drug development for different ultra-rare tumors. In the initial pilot phase (1 to 2 years), infrastructure would be built using one or two ultra-rare tumors with known undrugged driver mutations. A workshop would be convened with disease experts and stakeholders to analyze tumor biology and identify promising drug development approaches. With the assistance of the FNIH, the NCI would develop collaboration and IP agreements, establish a PPP Steering Committee and a PPP Scientific Advisory Board, and build the infrastructure for an open notebook platform. Once the

targeting approaches are decided, researchers from across government, academia, and industry would be leveraged to develop candidate drugs, and early-phase clinical trials would be initiated. A sustainability plan would be developed to ensure the long-term supply of drugs to patients, either through a for-profit or not-for-profit mechanism, depending upon the candidate, drug, and disease. After the initial pilot, the goal would be to begin new cycles every 1 to 2 years with new ultra-rare tumors and targets proposed by the community. With each cycle, the Scientific Advisory Board would be refined with the appropriate experts, and the open-data platform would illuminate the decision-making process, particularly regarding the FDA, to provide added value to all rare-tumor drug developers.

Many NIH programs exist that could be leveraged for drug development in ultra-rare tumors for compound identification and optimization, preclinical testing, understanding the natural history and molecular drivers, and conducting first-in-human trials in the cooperative trial networks. In discussions with several stakeholders during the past year, the NCI clarified that the proposed PPP is addressing an unmet need in ultra-rare tumors; focusing on well-established, undrugged vulnerabilities; establishing collaboration and IP agreements to promote drug approval and sustained supply for patients; developing a transparent, open-science paradigm across government, academia, and industry; and bringing together champions for ultra-rare tumors, biology mechanisms, and technology to rapidly develop drugs. The PPP is not competing with other efforts to develop rare-tumor therapies, focusing on therapeutic approaches not directly related to characteristic molecular alterations, or focusing on ultra-rare tumors without a clear molecular driver.

The August 2023 stakeholder meeting identified several themes for elements of success. These include requiring a strong, effective governance empowered to make decisions quickly, focusing on a small number of ultra-rare tumors at a time, having the infrastructure to move through projects quickly, establishing teams of "champions" for each project, adopting robust collaboration/IP agreements requiring minimal amendments, and having open notebook strategies that facilitate drug development. Several factors will determine which rare tumors to investigate and prioritize, including low incidence (less than 1 in 1 million) and well-defined diagnostic criteria; high mortality/morbidity with no effective therapies; untargeted, well-defined molecular drivers of tumorigenesis; and well-characterized experimental model systems.

Dr. Reilly commented on the value of rare-tumor research to all cancer patients. She emphasized that rare-tumor researchers must collaborate to be successful, and that those interactions may drive creative solutions to IP and collaboration barriers that could be adopted more broadly. Rare-tumor research has informed many of the hallmarks of cancer. Pathways to drug development and regulatory approval in rare tumors will be relevant to drug development in subtypes of common cancers. The NCI believes that this proposed PPP will address an unmet need in ultra-rare tumors and develop new paradigms and incentives for drug development.

Summary. Dr. Reilly summarized that MyPART has made substantial progress in engaging researchers and advocacy groups for the study of rare tumors and has established a strong foundation for the collection and analysis of linked clinical and molecular data on rare tumors. MyPART studies have resulted in the development of new, collaborative pediatric–adult interventional trials. MyPART is playing a key role in establishing national programs for rare-tumor research, particularly in collaboration with the CCDI, COG, and FDA. Dr. Reilly expressed appreciation to the MyPART team, collaborators, and patients. Drs. Widemann and Reilly are co-leaders of MyPART.

Questions and Answers

Dr. Richard J. Boxer, Clinical Professor, David Geffen School of Medicine, University of California, Los Angeles, asked about consideration for improving and mitigating the liability insurance issues with developing new medications for rare tumors. Dr. Reilly explained that this issue has been

noted in other discussions and that creative solutions would be needed, but the NCI is not necessarily in the position to provide those solutions.

Dr. Bertagnolli commented that MyPART is one example of public investments in the NCI Intramural Research Program that highlight what NCI can uniquely offer, augment work in the extramural community, highlight the synergies, and showcase the resources of the NIH Clinical Center.

NCAB Chair Dr. Carpten asked about the spectrum of rare tumors that tend to present more aggressively and have much higher mortality rates and the areas of focus for this research. Dr. Widemann explained that the NCI Clinical Center currently does not have any treatments to offer patients with aggressive rare rumors and would not have the capabilities to study them longitudinally. She noted the value of collaborating with extramural partners who are expert in this area and also noted the potential of the CCDI to build an infrastructure to enable and facilitate research challenging to do at some clinical sites. Dr. Reilly added that NCI's goals, through these new research efforts, will be to disseminate information to enable early diagnosis of rare tumors and build the knowledge base to better understand and focus on the more aggressive rare tumors.

In response to a question from NCAB Chair Dr. Carpten about prioritizing pediatric cancers and treatment approaches, Dr. Widemann responded that NCI's priority would focus on the greatest unmet need and also on seeking disease champions (i.e., principal investigators) who have already invested in researching a specific tumor, but have not been able to recruit a meaningful cohort to better understand the biology. Dr. Reilly noted that one of the goals of the PPP is that investigators would apply new technologies in their research.

Dr. Howard J. Fingert, Vice President, Medical Oncology, ONO PHARMA USA, INC., commented on the misperceptions that have led to barriers and decision-making about researching rare tumors and asked how barriers to IP could be addressed to advance collaborations with industry partners. Dr. Reilly anticipates that the open-notebook process would dispel some of the preconceived notions of why industry is deciding not to participate in this research.

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

Future Agenda Items. Members suggested a report on NCI efforts to protect the training of future cancer researchers and ESIs in the current budget environment; a review of the NCI Cancer Moonshot initiative's past, present, and future; an update on the Cancer Moonshot–funded Cancer Immune Monitoring and Analysis Centers (CIMACs) and their efforts in validating immuno-oncology biomarkers; an update on the future of the NCORP and its strategies for integrating the efforts of the Cancer Centers; and a report on the investments made by the NCI to support multi-cancer detection research. The NCAB members were asked to forward any further suggestions for potential future agenda items to Drs. Carpten and Gray.

VIII. 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.

IX. 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 discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was a potential conflict of interest, real or apparent.

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 2,241 NCI applications were reviewed requesting direct cost support of $927,557,453 and two FDA applications requesting direct cost support of $436,082.

X. 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 19th virtual meeting of the NCAB was adjourned at 5:20 p.m. on Wednesday, 6 September 2023.

Date	John D. Carpten, Ph.D., Chair, NCAB
Date	Paulette S. Gray, Ph.D., Executive Secretary