DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

8th Virtual Meeting of the BOARD OF SCIENTIFIC ADVISORS

Summary of Meeting

20 March 2024

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

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

BOARD OF SCIENTIFIC ADVISORS

SUMMARY OF MEETING
20 March 2024

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 8th virtual meeting on Wednesday, 20 March 2024, at 1:00 p.m. Dr. Shelton Earp, Director, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, and Director, UNC Cancer Care, UNC at Chapel Hill, presided as Chair. The meeting was open to the public on Wednesday, 20 March 2024, from 1:00 p.m. until 4:47 p.m. for the consideration of new requests for applications (RFAs) and Cooperative Agreements (Coop. Agr.) of new and re-issue concepts presented by NCI program staff.

BSA Board Members Present

Dr. Shelton Earp (Chair)
Mr. Timothy Babich
Dr. Suzanne J. Baker
Dr. Karen M. Basen-Engquist
Dr. Andrew T. Chan
Dr. Nelson J. Chao
Dr. Gloria D. Coronado
Dr. Mark P. Doescher
Dr. Chyke A. Doubeni
Dr. Jennifer R. Grandis
Dr. Trey Ideker
Dr. Michelle M. Le Beau
Dr. Ana Maria Lopez
Dr. Karen M. Mustian
Dr. Lisa A. Newman
Dr. Raymond U. Osarogiagbon
Dr. Sylvia Katina Plevritis
Dr. Erle S. Robertson
Dr. Cornelia M. Ulrich
Dr. Samuel L. Volchenboum
Dr. Robert H. Vonderheide

Board Members Absent
Dr. Chandrakanth Are
Dr. Dorothy K. Hatsukami
Dr. Richard C. Zellars

Others Present: Members of NCI's Scientific Program Leadership Committee, NCI staff, members of the extramural community, and press representatives.

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I. CALL TO ORDER AND OPENING REMARKS—DR. SHELTON EARP

Dr. Earp called to order the 8th virtual meeting of the Board of Scientific Advisors (BSA or Board) and welcomed current members of the Board, National Institutes of Health (NIH) and National Cancer Institute (NCI) staff, guests, and members of the public. Dr. Earp reminded the Board members of the conflict-of-interest guidelines and confidentiality requirements. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities, in writing and within 10 days, comments regarding items discussed during the meeting.

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

Dr. Earp noted that the next BSA meeting will be a joint meeting with the National Cancer Advisory Board (NCAB), scheduled for 11–13 June 2024, and will be held in person with remote participation available.

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

Dr. W. Kimryn Rathmell, Director, NCI, welcomed BSA members and attendees to the 8th virtual meeting of the BSA and provided a brief introduction, updates on training, the budget outlook and spending, and research highlights. Dr. Rathmell noted that with this meeting, she has now met with all six of NCI's Boards since becoming NCI Director and that she has a strong affinity with the BSA, having previously served as a member. Dr. Rathmell also noted that she values BSA's input; looks forward to robust discussions; and wants to hear opinions and ideas. She expressed appreciation to the BSA members for their contributions to NCI, noting that NCI recognizes the opportunity to receive tremendous insight from the Boards.

Introduction. Dr. Rathmell described her background as a physician–scientist and medical oncologist, noting that she values education and training. Eight years ago, she accepted a position as Hematology/Oncology Physician-in-Chief at Vanderbilt University Medical Center (VUMC) and then advanced to Chair of the Department of Medicine. She was interested in learning more about finance and pursued and completed a Master of Management in Healthcare from the Vanderbilt University Owen Graduate School of Business in 2022, thinking she would work in the health care administration field for the remainder of her career. These combined experiences have made her comfortable in her new role as NCI Director. Her path has led her to work with many advocates and patients, which also has been part of her joy in the work of NCI.

Dr. Rathmell noted three principles she values. The first is listening and openness, which she demonstrated with her listening tours across NCI divisions, and she now is moving those ideas into action. During those tours, she was transparent and provided the information the Boards would need to offer guidance to NCI. The second principle is teamwork and collaboration. The third principle is solving complex problems, which she credits as leading to her becoming a molecular biologist and working out a signaling pathway or a complex biological interaction.

Dr. Rathmell reflected on her career from its beginning in 2003 to becoming NCI Director, including educational and research components of varying priorities and clinical transitions (i.e., rotations). Two major roles were working on NCI's The Cancer Genome Atlas (TCGA) and beginning as a gerontology oncologist, specializing in kidney cancer at UNC Lineberger Comprehensive Cancer Center under the leadership of BSA Chair Dr. Earp. During her clinical career, she transitioned to being a renal cell carcinoma oncologist and then to a von Hippel-Lindau oncologist.

Dr. Rathmell explained that her research career began with studying hypoxia-inducible factor-1 (HIF-1) and HIF-2 metabolism under the direction of Dr. M. Celeste Simon at the University of Pennsylvania. This research and related discoveries were the topic of the 2019 Nobel Prize in Medicine. Drs. Simon and Rathmell were working with HIF-1/2 to better understand how cancer metabolism was being governed. Dr. Rathmell later started her own laboratory investigating transcriptional features of HIF-1/2 in this context while working in patient care. At that time, a conundrum about positron emission tomography (PET) imaging in renal cell carcinomas was that PET imaging was often "cold" or heterogeneous. The Rathmell laboratory conducted a series of PET studies. UNC at Chapel Hill invested in a magnetic resonance imaging PET machine, which was thought to resolve this issue but instead resulted in learning more about heterogeneity.

Dr. Rathmell and her laboratory became interested in understanding the difference between the metabolism and the cancer cells and their uptake of glucose in the environment that led to the immune cells being starved of this nutrient. They conducted a "tumor juice" project, evaluating the interstitial fluid and first discovering that glucose was in abundance for the cells being studied. Dr. Rathmell collaborated with Jeffrey C. Rathmell, VUMC immunologist, who has been a long-time immune metabolism investigator. They discovered that although a sufficient amount of glucose is available, it is not being used by the cancer cells *in vivo* or the T cells as much as it is being used by the macrophages. This finding has led to other studies, including the soon-to-be published data showing how kidney cancer cells are secreting cytokines that change the metabolic profile of the macrophages present in the microenvironment and the recently published data revealing that obesity influences the macrophages and their metabolic characteristics. Dr. Rathmell acknowledged the numerous students, postdoctoral researchers, and other colleagues who have been a part of this research.

NCI Training. Dr. Rathmell remarked that a cornerstone of her time at NCI will focus on trainee programs and early-investigator work, noting that the field cannot afford to lose a generation of scientists. NCI is empowering the next generation of cancer researchers through its individual and institutional awards and specific awards that promote diversity, from pre-doctoral to mid-career to established investigators. In addition, NCI has initiatives in place to accelerate early-stage investigators (ESIs) to achieve a first R01 grant and/or advance to an independent career. The NanCI by NCI is an artificial intelligence (AI) tool that introduces trainees to content of interest and connects them with researchers through networking. The *Inside Cancer Careers* podcast provides a source of information for trainees about how they fit into the broader cancer research environment. The Early Investigator Advancement Program (EIAP) focuses on ESIs and new investigators from minoritized groups who are conducting cancer research and assists them in grant writing and networking skills and helps to elevate the innovation and impact of their science to prepare them for applying for an R01 grant. EIAP will continue to work with the awardees to secure additional NIH funding. The results of the initial cohort are being reviewed, and updates will be provided at a future meeting. Last, NCI has self-paced data science training programs that enable investigators to learn to use essential data tools in their daily work.

NCI Budget Outlook and Spending. Dr. Rathmell noted that government shutdowns due to lapses in appropriations have been averted four times in fiscal year (FY) 2024, with four continuing resolutions (CRs), and that the current CR expires 22 March 2024, which is halfway through FY 2024. NCI has been working on interim grant policies based on FY 2023 appropriations and will confirm the paylines when a full budget is received. NCI is part of a complicated federal budget ecosystem, in which the appropriations from Congress cover a significant portion of the national landscape. A previous CR divided the appropriations bills into two funding groups; the Labor, Health and Human Services, Education, and Related Agencies (L-HHS), which funds NIH and NCI, will be in the second group to receive appropriations. Dr. Rathmell noted that Ms. M.K. Holohan, Director, Office of Government and Congressional Relations, NCI, will provide further details on the NCI FY 2024 budget.

BSA members were reminded how NCI spends its appropriations. Dr. Rathmell explained that NCI's FY 2023 budget was $7.3 billion (B) and that the Research Project Grant (RPG) pool is the largest investment of NCI funding, at 44 percent of the total budget in FY 2023. In addition, 18 percent of NCI's budget supports intramural research; 7 percent funds research management and support, and 8 percent supports NCI-Designated Cancer Centers (Cancer Centers) and Specialized Programs of Research Excellence (SPOREs). Most of the funding to RPGs, SPOREs, and other grants supports 5-year or 7-year awards. NCI's budget is committed, and any available funds are dictated by the appropriations. Since FY 2019, the NCI has been funding an increasing number of extramural awards. Approximately 25 percent of grants awarded during this period were RPGs. The number of NCI modular awards progressively decreased from 63 percent to 17 percent. NCI decreased the budgets of these awards by 8.5 percent. During this same period, the number of NCI nonmodular awards increased from 39 percent to 80 percent.

NCI submits a Professional Judgment Proposal (also called the Bypass Budget) directly to Congress. This Bypass Budget estimates the cost of the work that the NCI is expected to perform. Inflation has been increasing more than the budget estimates for several years. Already behind, the NCI has been asked to implement new initiatives and aims to improve cancer health care. The Annual Plan and Budget Proposal for Fiscal Year 2024, which the President considers before recommending a budget, was increased to $9.9 B. For the 2025 Professional Judgment Budget, the NCI is proposing a budget increase to $11 B, which reflects inflation and projected costs for such efforts as conducting clinical trials, gathering and analyzing cancer data, and using the data. The FY 2025 President's Budget Proposal was released on 11 March 2024 and includes $7.8 B for NCI discretionary spending and proposes $1.4 B of mandatory funding for the Cancer Moonshot℠. With an increase in appropriations, NCI could innovate more in clinical trials, take on projects that address environmental health and cancer, and do more in the cancer data space.

Dr. Rathmell explained that NCI has been expecting a "flat" FY 2024 budget, which amounts to a reduction. NCI is challenged to maintain current efforts for several reasons. The 21st Century Cures Act funding ended in FY 2023, and the $216 million (M) appropriation for the Cancer Moonshot has not been continued. Research costs and salaries increase. The government-directed salary increase for the intramural program alone was more than $40 M. Nonnegotiable expenses for NCI increase annually by $75 M to $100 M. The RPG cost increases by $250 M annually to fully fund awards at the current level. To manage a constrained budget, 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 Cancer Center Support Grants (CCSGs) and cancer training awards, as well as for the noncompeting CCSGs. Cuts to the intramural research program are anticipated to be along the same levels as cuts to extramural awards. A hiring pause in the intramural program has been implemented, and contractor utilization and programs that have reached their life span are being reviewed. Additional information about NCI budget and appropriations can be found on the NCI website, including the updated Budget and Appropriations page and NCI's *Bottom Line: A Blog about Grants and More*.

Research Highlights. Dr. Rathmell highlighted recent progress in cancer research. The National Cancer Plan (NCP) was implemented in 2023 and is a roadmap for defining the cancer agenda for the nation. The NCP is a useful tool and has a process for annual evaluations. The President's Cancer Panel evaluates and provides feedback to the nation on the plan. This evaluation offers guidance for the White House, Congress, NCI, and other federal agencies on how to achieve the goals of the NCP. These goals encompass preventing cancer, detecting cancers early, developing effective treatments, delivering optimal care, eliminating inequities, maximizing data utility, optimizing the workforce, and engaging every person.

President Joseph R. Biden announced the reignited Cancer Moonshot 2 years ago as an all-of-government approach to pull discovery science and translation together and ensure that everything is getting into the hands of patients so that we make a bigger and more meaningful impacts on patient outcomes. The bold but achievable goals are to reduce the U.S. cancer death rate by 50 percent by 2047 and to improve the experience of patients with cancer and their families. Dr. Rathmell noted that cancer mortality rates are declining, with recent decreases more substantial than in past decades. Studies that address access and apply discoveries to patient care hold potential to improve the experience of patients with cancer.

NCI has achieved numerous accomplishments in cancer research. A detailed list can be accessed online at *Cancer Currents: An NCI Cancer Research Blog*. Tumor-infiltrating lymphocytes for advanced melanoma is the first Food and Drug Administration–approved cellular therapy for solid tumors. This advance in research and treatment is attributed to decades of work by Dr. Steven A. Rosenberg, Chief, Surgery Branch, Center for Cancer Research, NCI, and other laboratories throughout the country. This effort promotes cellular therapy to a position where it can be applied across many fields. In January 2024, during the White House Cervical Cancer Forum, NCI announced the launch of the Self-Collection for HPV Testing to Improve Cervical Cancer Prevention (SHIP) Trial Network, which aligns with the NCP goal of early detection. The SHIP Trial Network was developed in collaboration with federal and private-sector partners and patient advocacy groups, all addressing disparities. The groups selected to pilot the SHIP Trial Network have populations that need access to testing for human papillomavirus (HPV) for proper risk assessment and effective care management. SHIP directly works with the community, which aligns with the NCP goal to engage every person.

NCI launched its first large-scale Cancer Screening Research Network (CSRN). Dr. Rathmell noted that the goal is to build a network dedicated to life-saving interventions that starts with screening patients. Some of the most significant improvements in cancer can be made in this area, particularly at the population level, to achieve the goal of reducing cancer mortality by 50 percent by 2047. The initial study in the CSRN is evaluating a multi-cancer detection blood test to better understand early detection based on blood biomarkers and how to interpret that information. In February 2024, NCI announced the Virtual Clinical Trials Office Pilot Program. The aims are to improve rates of accrual to and retention in trials, address staffing challenges, and reduce the burden of clinical research, particularly for sites that do not have strong infrastructure. The key feature is centralized remote staff support for NCI-sponsored clinical trials. NCI selected six U.S. sites from among the Cancer Centers and NCI Community Oncology Research Program (NCORP) to participate in the pilot program.

The Childhood Cancer Data Initiative (CCDI), which is a direct result of the initial Cancer Moonshot, is making progress in helping children with cancer and their doctors obtain the data that they need. A component of the CCDI is the Molecular Characterization Initiative, which provides state-of-the-art molecular characterization of pediatric tumors at the time of diagnosis to inform optimal treatment decisions. Insights about pediatric tumors gained through the Molecular Characterization Initiative can potentially change patients' lives.

NCI partners with Cancer Research UK to sponsor the Cancer Grand Challenges. The goal is to assemble bold groups to tackle new challenges in cancer. Each internationally collaborative team receives up to $25 M over 5 years. Four new challenge areas were announced in March 2024 in the topic areas of reducing cancer inequities, understanding mechanisms of early-onset cancers, developing drugs for solid tumors in children, and broadening knowledge about how T cells recognize cancer cells.

In closing, Dr. Rathmell solicited the BSA members to provide input on what areas they would like to hear more or less about, research areas that NCI should prioritize in the RFAs, and resourcing programs during limited funding. She noted that NCI is planning an annual retreat to discuss priority-setting and will be inviting the chairs of its six Boards to attend. Dr. Rathmell pointed out that although the budget

outlook is not ideal, innovative solutions can emerge in the face of challenging circumstances. NCI will operate creatively, collaboratively, and efficiently to steward the resources for this fiscal year. NCI's ultimate goal is to benefit all people, patients, and families affected by cancer, and it will use the NCP as the roadmap to achieve the Cancer Moonshot goals of ending cancer.

In the discussion, the following points were made:

- NCI recognizes that the $500,000 awarded for R01 grants has not been increased in some time. A trade-off exists between the amount awarded per grant and the number of grants that can be funded. The decision was made to offer additional prizes. The impact of raising the amounts of those grants will be modest because modular awards are common.

- An opportunity exists to consider supplementing the R01 funds with sources from other NIH institutes and centers (ICs).

- The BSA appreciates NCI's approach and strategy for funding research, particularly given the current budget environment. Reducing support for training grants would have the most detrimental effect on workforce development and pathways that engage the next generation of cancer researchers.

- Some Cancer Canters are collaborating to offer programs that can help the next generation of cancer researchers and may serve as a model for training grants.

- Training grants are essential for aiding principal investigators who are facing cuts to their funding budgets, and they should be given top priority.

- Cancer research and improved outcomes have the potential to benefit many people. Exploring the possibility of partnering with payers, industry, and the business sector should be considered.

- The new Virtual Clinical Trial program could be a means of expanding services to broader areas of the communities that are beyond the limited geographical reach of Cancer Centers.

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

Ms. Holohan reported on FY 2024 appropriations and shared updates from the 118th Congress. Since November 2023, half of the 12 spending bills required for FY 2024 have been signed into law. However, the six remaining bills, the L-HHS; Defense; Financial Services and General Government; Homeland Security; Legislative Branch; and State, Foreign Operations, and Related Programs bills, have not yet been passed by Congress. Agencies funded by these six bills (including NCI and NIH) are currently being supported by a continuing resolution (CR) that provides funding at FY 2023 levels through March 22, 2024. A partisan dispute over border issues and funding for the Department of Homeland Security is stalling the process further.

The President's FY 2024 budget request proposed an overall level of $48.6B for NIH, a $920M increase over the FY 2023 enacted level. The NIH total included $7.8B for the NCI, which would continue the ongoing FY 2023 level of funding of $216M for the reignited Cancer Moonshot, and provided an additional $500M for FY 2024. The Fiscal Responsibility Act (FRA), a law that caps FY 2024 nondefense discretionary spending at FY 2023 levels, was passed June 2023 as part of a bipartisan agreement to raise the debt ceiling. The FRA allowed defense discretionary spending to increase by 3 percent (the amount proposed in the President's FY 2024 budget) and stipulated a 1 percent increase in FY 2025 for both defense and nondefense discretionary spending. The FRA includes an automatic spending cap with a 1 percent across-the-board reduction that is triggered by failing to pass all FY 2024 spending bills by 1 January 2024. This 1 percent cut will become permanent if the remaining bills are not

passed by 30 April 2024.

Shortly after enactment of the FRA, House Republicans announced that they would treat the FRA budget caps as "floors, not ceilings" and write their appropriations bills to the FY 2022 funding level, approximately $130B below the FY 2023 enacted funding level and $119B less than the agreed-upon FRA level. In July 2023, the House bill proposed a total of $44.7B for NIH, which is approximately a $3B reduction from the current level. The NIH total included $7.1B for NCI, which does not include continued funding for the Cancer Moonshot, an overall proposed decrease of $216M. The bill also proposes that at least a dozen health programs be eliminated, as well as the Agency for Healthcare Research and Quality. The Senate Appropriations Committee's bill (approved in June 2023) included $47.8B for NIH, an increase of approximately $123.6M from current funding levels. The bill proposes $7.3B for NCI, which would include a $276M increase from the FY 2023 enacted level, including a total increase of $60M for the NCI base budget and $216M for the Cancer Moonshot. Ms. Holohan reminded the BSA members that in FY 2020 congressional appropriators backfilled the NCI budget gap when NIH experienced a significant decrease in Cancer Moonshot funding levels between FY 2019 and FY 2020.

Ms. Holohan noted that the President's FY 2025 budget proposal (released on 11 March 2024) allocates $50.1B for NIH, an increase of $2.4B over the FY 2023 enacted level. The NIH total includes $7.8B for NCI discretionary spending (an increase of approximately $500 M over the FY 2023 level) and a mandatory proposal of $1.5B for the Cancer Moonshot. Ms. Holohan reminded the BSA members that the President's budget request begins the appropriation process. Following the announcement of President Biden's FY 2025 budget request, Office of Management and Budget Director, Shalanda Young, and the Secretary of Health and Human Services (HHS), Xavier Becerra, have testified on the budget request before congressional committees. House and Senate appropriations hearings for NIH have not yet been scheduled; Ms. Holohan noted that the House did not hold a traditional NIH appropriations hearing for the FY 2023 budget request, instead they conducted more of an oversight hearing, including witnesses from CDC and HHS along with then-acting NIH Director Dr. Larry Tabak. She added that while the President's budget request begins the appropriations process, but that congress controls spending levels and final appropriations decisions. She also noted that historically appropriators tend to be less partisan than many other congressional committees, after all, they need to come together to pass legislation every year. She also pointed out that the relatively recent return of earmarks (with transparency and a focus on public-sector projects as schools, roads, bridges, and cancer centers) provides incentives for appropriators to be vested in finishing spending bills.

Ms. Holohan highlighted several congressional retirements and departures. Nearly 60 members of Congress (49 Representatives and 8 Senators) have announced that they will not seek re-election in 2024 or have left office early. With some members departing before the end of their current terms, House Republicans have a slimmer majority over Democrats for passing partisan legislation. House Committee on Energy and Commerce (E&C) Chair Cathy McMorris Rodgers (R-Washington), plans to retire at the end of her term in 2024. E&C Subcommittee on Health Ranking Member Anna Eshoo (D-California) announced that she will retire from Congress in 2024, at the end of her 16th term in the House. Representative Barbara Lee (D-California) is running in California's Senate race, and Senator Joe Manchin (D-West Virginia) will not seek re-election in 2024; both are House L-HHS Appropriations members. The House Appropriations Chair, Representative Kay Granger (R-Texas), announced that she will retire from Congress at the end of her term, but will step down as Chair as soon as the FY 2024 process is complete, opening a top position on the committee. Notably for the cancer research community, both Congressmen Derek Kilmer (D-Washington) and Brian Higgins (D-New York), Co-chairs of the House Cancer Caucus, will also be retiring from the House.

Members were informed that Dr. Rathmell has been actively engaging the White House and members of Congress. She has also met with many Senate appropriators, including Chair Tammy Baldwin (D-

Wisconsin), Ranking Member Senator Shelley Moore Capito (R-West Virginia; Senator Jerry Moran (R-Kansas); Senator John Boozman (R-Arkansas); Senator Jack Reed (D-Rhode Island) and Senator Tammy Baldwin (D-Wisconsin), Chair, L-HHS Appropriations. Ms. Holohan ended her presentation with a suggestion that BSA members work with their institutions to share their research efforts with not only their congressional delegations but also with professional associations to explain their findings, describe ongoing research questions, and to explain how NCI funding supports their work.

In the discussion, the following points were made:

- The 1 percent across-the-board reduction stipulated by the FRA would not become permanent if the remaining bills are passed before the 22 March 2024 deadline.
- The most likely scenario for the FY 2024 appropriations for NCI is a flat budget, possibly with some additional funding to compensate for the $216M decrease as Cancer Moonshot funding ended in FY 2023.

IV. AUTOMATED HEART-HEALTH ASSESSMENT FOR CANCER SURVIVORS— DR. KATHRYN E. WEAVER

Dr. Kathryn E. Weaver, Professor, Departments of Social Sciences and Health Policy and Implementation Science, Wake Forest University School of Medicine, and Associate Director of Population Sciences, Atrium Health Wake Forest Baptist Comprehensive Cancer Center, reported on cardiovascular (CV) health assessment for post-treatment survivors. The overarching goal of her research is to reduce the burden of cardiovascular disease (CVD) among post-treatment cancer survivors using informatics tools embedded in oncology. Cancer survivors have almost twice the risk of fatal heart disease compared with the general population, and deaths related to heart disease exceed primary cancer deaths for many common cancer types. This heightened risk among survivors is due to several factors, including the shared mechanisms of cancer and CVD, adverse changes in lifestyle factors during cancer treatment, and cardiotoxic effects of certain cancer treatments. Accordingly, clinical practice guidelines recommend CVD risk assessment and counseling for cancer survivors.

An analysis performed by Dr. Weaver suggests that a large proportion of survivors seen in community settings would benefit from such CV assessment. A high burden of CV risk was observed in an analysis of 502 mostly female patients seen for routine follow-up of primarily breast and endometrial cancers. Although most survivors had an ideal smoking status, many had American Heart Association (AHA) Simple 7 CV factors that were categorized as intermediate or poor. Several of the factors were not known to the study participants and not reported in the electronic health record (EHR). Dr. Weaver noted that this study highlighted the challenge of acting without a complete understanding of CV health. Therefore, data visualization and clinical decision support tools have an important role in assisting outpatient oncology providers in delivering guideline-recommended care to reduce CVD burden among post-treatment cancer survivors.

Dr. Weaver's team adapted the Automated Heart Health Assessment (AH-HA) tool from an existing primary care tool with input from both oncology providers and cancer survivors. The tool renders a visual, interactive display of the AHA Simple 7 CV health factors automatically populated from a patient's EHR. The factors are color coded red, yellow, and green to enable busy clinicians to address priority areas quickly. The tool includes a tab indicating receipt of cancer treatments with cardiotoxic potential, which was added to provide critical treatment context. The tool is launched via a best practice advisory in the EHR, and providers receive training to support its use as part of routine care for survivors.

The effectiveness of AH-HA was assessed in a randomized hybrid effectiveness implementation clinical trial within the NCORP network. Cancer survivors receiving routine follow-up care 6 months after

potentially curative cancer treatment were enrolled. The 645 participants included survivors of several common cancers with significant competing mortality risk from CVD (e.g., breast cancer, prostate cancer, colorectal cancer, endometrial cancer, lymphomas). More participants were women with breast cancer, with smaller numbers of other included cancers. On average, the participants were 3.5 years post-diagnosis. The trial randomized nine NCORP practices that used the Epic EHR to the AH-HA tool or usual care. Patients were enrolled and completed a brief baseline assessment prior to a routine outpatient oncology visit. They completed the visit with access to the tool only at AH-HA intervention sites. Immediately after this visit, the patients completed a second survey asking about the visit and topics discussed with their provider. Cardiovascular documentation and referrals were assessed, and participants were followed for 12 months through surveys and EHR review.

The primary outcome of the trial, participant-report discussion of at least one non-ideal or missing CV health factor, was doubled among survivors receiving the AH-HA intervention compared with the group that received usual care. Notably, none of the participants had all CV health factors categorized as ideal; all factors were actionable and warranted a discussion with their provider. Almost four times as many factors were discussed and documented in intervention clinics relative to controls, and referrals to primary care were increased. Providers reported high satisfaction with the tool across several domains. The trial results suggest that AH-HA is effective at promoting CV health discussions during routine follow-up care of cancer survivors. Follow-up data collection recently has been uploaded by computer, and results for longer-term effects should be available soon. Dr. Weaver's team is building on these findings in several ways. AH-HA is being upgraded to reflect provider feedback, including the addition of sleep as an additional CV health metric. A follow-up pragmatic trial with additional NCORP sites is being planned to extend the reach of the intervention to a broader population of patients and providers and to examine implications for health equity. Discussions are being held to implement the tool on multiple campuses of the Atrium Health Wake Forest Baptist Comprehensive Cancer Center. Dr. Weaver thanked the exceptional teams at both the academic and NCORP sites and acknowledged significant support from NCI.

In the discussion, the following points were made:

- Research projects that address overlapping areas of interest (e.g., cancer and CV health) were identified as a funding priority.

- Breast cancer can predominate in multicancer studies. Efforts to recruit patients from other cancer populations are being expanded.

- Patient populations in the AH-HA trial accurately represented the patient populations observed at participating NCORP sites. With busy providers and other potential barriers, patient counseling remains a significant challenge. Efforts are being made to incorporate relevant information into patient portals and to connect patients who have the highest risk to available resources.

- Follow-up efforts will determine whether the AH-HA tool increased coordination of oncology care and primary care. Dr. Weaver's team is interested in using AH-HA to improve communication between the two teams.

- Provider training for the AH-HA tool comprised two 30-minute sessions. One session focused on the connection between CV health and cancer; the second session focused on tool functionality and guiding the discussion with patients after using the tool.

- Information technology (IT) engagement was the main reason cited for NCORP sites' not participating in the AH-HA study. The capacity to perform IT-adjacent interventions should be

improved within the NCORP sites.

V. RFA/COOP. AGR./LIMITED COMPETITION CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

Division of Cancer Biology
RNA Modifications Driving Oncogenesis (RNAMoDO) (New RFA/Coop. Agr.)—Dr. Stefan Maas

Dr. Stefan Maas, Program Director, Division of Cancer Biology (DCB), NCI, presented a new RFA concept on RNA Modifications Driving Oncogenesis (RNAMoDO). The goal is to support mechanistic research on RNA modifications driving oncogenesis through translational reprogramming. Cancer cells are exposed to stress across the cancer stages, from transformation to chemoresistance. The dynamic modification of RNAs is reshaping the translatome and is emerging as a key tool for cancer cells to adapt and survive. RNA epigenetics affects various RNA species, and approximately 100 types of modifications exist in humans. These modifications alter RNA processing, structure, stability, and transport. In cancer, changes in modifications or in the machinery that introduces, removes, or recognizes these modifications have been linked to oncogenic and tumor-suppressive roles. Recent insights point to a central role for modifications in messenger, transfer, and ribosomal RNAs (mRNA, tRNA, rRNA, respectively) in promoting cancer development through translational reprogramming. Examples include N7-methylguanosine (m7G) modification of specific tRNAs in glioblastoma and liposarcoma and N7-methyladenosine (m6A) modification of mRNA in acute myeloid leukemia. In addition, modification of rRNA (m1acp3ψ) has been observed in 45 percent of colorectal cancer cases.

This concept builds on insights from recent activities and developments across NCI and NIH, including the 2020 DCB workshop on "RNA Epitranscriptomics in Cancer"; 2023 National Science Foundation (NSF),National Human Genome Research Institute (NHGRI) RNA tools funding opportunity; 2023 National Academies of Sciences, Engineering, and Medicine (National Academies) consensus study "Toward Sequencing and Mapping of RNA Modifications"; and 2022 and 2023 notices of special interest (NOSIs) for exploratory and technology development projects on RNA modifications in cancer biology.

A portfolio analysis of active NCI grants on RNA modifications revealed that only 3 of the 29 R01-type grants are investigating the impact on translational regulation in cancer, no funded project is examining tRNA modification, and no grant is investigating the interplay among RNA modifications. By comparison, more than 200 funded R01-type NCI grants are evaluating DNA epigenetics, despite the much smaller number of DNA modification types.

Dr. Maas reiterated that the goals of the RNAMoDO program will be to promote mechanistic investigations into the mRNA, tRNA, and rRNA modifications that are driving oncogenesis through translational reprogramming; decrease fragmentation and siloing regarding modification types and RNA species; attract top RNA modification researchers to cancer biology; foster collaborative research on interactions between modifications; and build on and integrate exploratory research and technology development. This program also will link to existing NCI programs, advance the goals of the NCP, and promote outreach and the training of the next generation of researchers. This RFA will be responsive to multiple or single principal investigator U01 projects, addressing essential expertise in RNA modifications, translational regulation, and cancer biology. The program evaluation will analyze progress in achieving the goals, particularly on the level of collaborations across RNA species and modification types, program productivity, and role in advancing progress in the field.

Subcommittee Review. Dr. Michelle M. Le Beau, Arthur and Marian Edelstein Professor Emerita of Medicine, Director Emerita, University of Chicago Comprehensive Cancer Center, and Chief Scientific Officer, Cancer Prevention and Research Institute of Texas, expressed the Subcommittee's strong support for the concept, which is timely and addresses gaps in knowledge. Dr. Le Beau highlighted that this

concept represents an appropriate progression from the more descriptive science of RNA abnormalities that have been supported by the R03 and R21 NOSIs to a focus on developing technology and describing those RNA abnormalities in cancer. The Subcommittee noted the opportunity to focus on mechanistic studies and interactions between RNA modifications that altered the transcriptome in cancer and emphasized promoting collaborations both within this program and across existing NCI initiatives, including the Cancer Systems Biology Consortium (CSBC) and the Translational and Basic Science Research in Early Lesions (TBEL) network.

In the discussion, the following points were made:

- Given the current budget outlook, NCI can consider mechanisms to share costs with other ICs (e.g., NHGRI) and/or organizations, including graduate medical schools or NSF, in the future.
- An NIH-wide interest group on RNA modifications is pursuing collaborations with other agencies and ways to advance ideas, such as the Human RNome Project.
- This concept is highly focused on cancer biology and is a specialized initiative that would work in parallel or complementary with other efforts that perhaps are started in other ICs.
- The scope of the RFAs should be expanded to include investigations of RNA modifiers, such as human methyltransferase-like 3 (MTTL3) involved in oncogenesis.

The first-year cost for the one-time issuance is estimated at $4.9M for five U01 awards, with a total cost of $24.5M for 5 years.

Motion. A motion to approve the DCB's new RFA/Coop. Agr. entitled "RNA Modifications Driving Oncogenesis (RNAMoDO)" was approved unanimously.

Office of the Director
Youth Enjoy Science (YES) Research Education Program (Re-Issue RFA)—
Drs. Belem López and Sangeeta Ghosh

Dr. Belem López, Program Director, Center to Reduce Cancer Health Disparities (CRCHD), NCI, presented the re-issue RFA concept to continue the Youth Enjoy Science (YES) Research Education Program (R25). Dr. Lopez informed members that the R25 YES Program was established in 2016 as a component of Continuing Umbrella of Research Experiences (CURE) and supports middle school, high school, and undergraduate students and their teachers. YES encourages students to consider a possible career in the biomedical field and provides them with the skills necessary to pursue a career in science. YES promotes effective early intervention strategies to engage precollege and college students from diverse backgrounds in research experience, curriculum and methods, and outreach. The objective is to encourage their interest in biomedical sciences and cancer research, help them envision cancer research as a career path, and strengthen their practical research and career skills.

Each YES application requires three activities. The first activity is research, which can be individual or mentored research experiences for high school or college students. The second activity is curriculum and methods, in which teacher and faculty participants can develop cancer-related activities for the classroom. All education activities should be relevant to cancer. The third activity, unique to this R25, is outreach that provides meaningful engagement with families, teachers, and communities. Since the inception of YES, the NCI has received 212 applications and made 27 awards, including 4 renewals. The individual YES sites are represented across 21 states and include five Institutional Development Awards (commonly called IDeA) states. The YES Program is serving as an early intervention STEM program; is reaching and supporting rural communities, Native American communities, and states with lower amounts of NIH

funding; and is addressing cancer health disparities and increasing community engagement. In the past 2 years, the funded impact scores ranged between 10 and 13. Funding decisions for FY 2024 are pending.

Dr. López detailed the accomplishments and contributions of the YES Program. A program assessment of the R25 YES awardees was conducted encompassing FY 2018 to FY 2023 and across three goals. Specifically, the goals are: 1) create and maintain programs to engage grades 6–12 and/or undergraduates from underrepresented minorities in cancer research experiences. The YES awardees trained 2,584 students. Alumni pursued science and biomedical-related degrees, including medical school and cancer biology doctoral programs; 2) develop cancer educational tools for students and develop novel instructional approaches to improve science teaching. The University of Alabama at Birmingham YES established a cancer biology undergraduate major and several courses, including oncogenes, tumor suppressors, hallmarks for cancer, and cancer health disparities. The University of Pittsburgh YES created a social media virtual learning environment via Discord and a cancer curriculum that provided experiential training in social determinants of health. Teacher trainees developed curricula on stomach cancer and inherited cancer, received research experience in wet labs, and published a special issue in *STEM Outreach*.; and 3) enhance science/health education; disseminate biomedical, behavioral, and clinical research; and expose students to various aspects of cancer research. Principal investigators developed Talking Circle sessions in the Cancer Primer course to regularly update parents. The University of Maryland, Baltimore YES used Arnstein's Ladder of Citizen Participation to empower communities to have action in program organization and operations to promote durable change and support the success of scholars. Some YES R25 awardees have conducted outreach to both elementary and middle school trainees and families about cancer concepts. Overall, the YES Program has increased knowledge of cancer research skills, critical thinking skills, and cancer risk factors and disparities.

In addition, the assessment revealed that 24 percent of trainees were Black/African American, 19 percent were Hispanic/Latino, and 12 percent were Native American. The majority of trainees were female. The R25 YES trained 182 teachers and is highly competitive, with a minimum 4 percent admission rate at some sites. Additionally, a significant impact was made in recruiting and reaching underrepresented students. A data set of trainee diversity was compiled that included 2020 U.S. Census Bureau data for each county where different R25 YES institutions are located. This cross-reference confirmed that the YES Program is engaging the hard-to-reach underrepresented populations, including Black/African American trainees, Native American trainees, and individuals from low socioeconomic backgrounds.

Dr. López highlighted that the YES Program also made important scientific contributions during this funding cycle. YES investigators published 88 papers, had two edited volumes on *The Cancer Crisis in Appalachia: Kentucky Students Take Action*, produced seven podcasts featuring principal investigators and trainees, and appeared in three television feature stories on the local and national levels. She informed members that this RFA re-issuance will continue to support the aims of the YES Program and will increase the number of YES applications and awards from across the nation, especially from states that receive less funding from NIH. Additionally, this initiative aligns with the NCP goals to grow and increase diversity in the cancer research workforce.

Subcommittee Review. Dr. Ana Maria Lopez, Professor, Medical Oncology and Integrative Medicine and Nutritional Sciences, Director, Integrative Oncology, and Associate Director, Diversity, Equity, and Inclusion, Sidney Kimmel Cancer Center,Thomas Jefferson University, expressed the Subcommittee's enthusiasm and support for the concept. The Subcommittee commended NCI on an exceptional precision educational intervention and a highly competitive program and emphasized expanding the program to include elementary school students.

In the discussion, the following point was made:

- Youth who live in rural or frontier areas that are geographically located some distance away from any opportunity at a biomedical institution also are underrepresented in the cancer research workforce and would benefit from the YES Program.

The first-year cost for the one-time issuance is estimated at $4.32 M for up to 12 R25 awards, with a total cost of $25.9 M for 5 years.

Motion. A motion to concur on the re-issuance of the OD's RFA entitled "Youth Enjoy Science (YES) Research Education Program" was approved with 20 ayes, 0 nays, and 1 abstention.

Division of Cancer Control and Population Sciences
Addressing Barriers to Health Care Transitions for Survivors of Childhood and Adolescent Cancers (STAR Act) (New RFA)—Dr. Lynn Adams

Dr. Lynn Adams, Program Director, Division of Cancer Control and Population Sciences (DCCPS), NCI, presented a new RFA concept for Addressing Barriers to Health Care Transitions for Survivors of Childhood and Adolescent Cancers. Dr. Adams informed members that although pediatric cancer survival rates and outcomes have substantially improved, work remains in addressing the needs of this population, particularly as they transition into adult health care settings. This concept is in direct response to Section 201A of the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Reauthorization Act, which was reissued in 2023. This Act states that NCI will support research to evaluate model systems of care for pediatric cancer survivors, including their transition to adult care and care coordination. The childhood cancer research advocacy community identifies this as a pressing need.

Reports show that from 1985 to 2015, medically excessive deaths (i.e., deaths above the expected that could have been averted) in the pediatric population 10 years or more after a cancer diagnosis increased and can be attributed to the late effects of treatment, new primary cancers, or recurrences not identified early. One major factor related to these deaths is inadequate follow-up care. The National Academies and the Children's Oncology Group (COG) recommend that survivors engage in lifelong follow-up care to monitor late effects of their previous cancer and treatments. Recently, COG surveyed its institutions about the transfer from pediatric to adult care and found that 50 percent were required to discharge survivors at an age cutoff between 18 and 26 years. Resources to support care transfer are generally lacking. Most of these institutions had no methods or patient navigators to facilitate the transfer to an adult provider.

Dr. Adams noted barriers and challenges to care transition. Pediatric cancer patients need comprehensive support, whereas adults manage and coordinate their own care. Pediatric cancer survivors require multidisciplinary care based on their specific cancer treatment and potential for late effects, and are vulnerable when they need to transition from pediatric oncology to adult health care settings. Challenges in transitioning to adult care exist on the individual patient level, such as difficulty navigating the health system and limited self-management and self-advocacy skills, and on the provider and health system level and can include lack of coordination and collaboration, resources, or insurance coverage. These barriers become more apparent in populations that experience health disparities.

In 2018, Congress passed the Childhood Cancer STAR Act. NCI responded with the following RFAs: RFA-CA-19-033, which established an investigator network for testing interventions to address adverse physical and psychosocial effects on survivors of pediatric and adolescent cancers, and RFA-CA-20-027 and RFA-CA-20-028, which solicitated applications proposing mechanistic, observational, or intervention studies to improve the care and quality of life of childhood cancer survivors. The response to these RFAs has been robust, but none examined the transition to adult care. In addition, of the 80 funded awards in NCI's portfolio on pediatric or adolescent and young adult survivorship in the last 5 years, only 1 focused on transition to adult care.

The Childhood Cancer STAR Reauthorization Act creates a new opportunity for NCI to support research that benefits lifelong care for cancer survivors. This RFA will solicit R01 applications proposing intervention studies that address barriers to care transition for this population at the individual and system levels. The applications must focus on the development, testing, or evaluation of interventions; include a multidisciplinary research team; and describe a plan for potential scalability and sustainability. NCI encourages applications that include diverse populations, address the impact of social determinants of health on transition, and propose multilevel studies.

Subcommittee Review. Dr. Suzanne J. Baker, Associate Director of Basic Sciences, St. Jude Comprehensive Cancer Center, and Endowed Chair in Brain Tumor Research, St. Jude Children's Research Hospital, expressed the Subcommittee's enthusiasm and strong support for the concept. Dr. Baker noted that this concept will be critical to complementing the existing impact of the STAR Act. The Subcommittee emphasized incorporating the multidimensional issues that will need to be considered in this research, disentangling the specific age-related transitions, and reviewing payment mechanisms.

In the discussion, the following points were made:

- A phased funding mechanism would be best to ensure that the RFA, which focuses on health care transitions, reflects the integration of existing programs and initiatives.

- NCI assembles a Special Emphasis Panel (SEP) to review the concepts specific to the initiative; whereas, the NIH Center for Scientific Review (CSR) utilizes established Study Sections.

- The RFA will call attention to or describe the existing resources in this research area across NCI programs that applicants can complement but not duplicate.

The first-year cost for the one-time issuance, with two receipt dates, is estimated at $4M for 5 R01 awards and $6M for up to 7 R01 awards in the second year, with a total cost of $50 M for 5 years.

Motion. A motion to approve the DCCPS' new RFA entitled "Addressing Barriers to Health Care Transitions for Survivors of Childhood and Adolescent Cancers (STAR Act)" was approved unanimously.

Division of Cancer Prevention
Cancer Prevention Clinical Trials Network (CP-CTNet) (Re-Issue RFA/Coop. Agr.)—
Dr. Eva Szabo

Dr. Eva Szabo, Chief, Lung and Upper Aerodigestive Cancer Research Group, Division of Cancer Prevention (DCP), NCI, presented a re-issuance concept to continue the Cancer Prevention Clinical Trials Network (CP-CTNet). Dr. Szabo informed members that early phase clinical trials are a critical component of DCP's drug development pipeline, and CP-CTNet is one component of this pipeline that provides a unique service in performing the preliminary safety and efficacy of early phase clinical trials. She noted that the objectives of this program are to qualify cancer-preventive agents for further clinical development and to make this process more efficient. The main goals are to optimize clinical trial designs and develop surrogate and intermediate endpoint biomarkers. CP-CTNet was established in 2019, has an accrual rate of approximately 250 participants annually, and has 29 active studies in various phases of development.

Dr. Szabo highlighted recently completed studies. Erlotinib administered weekly, as opposed to daily, resulted in a 30 percent decrease in duodenal polyp burden in the familial adenomatous polyposis (FAP) cohort. FAP is an autosomal-dominant polyposis syndrome. The next step, a Phase III trial, is under discussion. Exemestane, which is effective in reducing the risk of breast cancer, evaluated alternative

dosing schemes of three times per week versus once per week and was compared with the standard daily dosing to examine the effects on serum estradiol. The results showed that the three times per week intervention was noninferior to the daily intervention and was well tolerated. The next step will be to conduct a longer study, which is currently funded by the Breast Cancer Research Foundation. Following favorable results in this longer study, a Phase III trial will be planned under the management of NCORP. She noted the progress of two ongoing trials that focus on Lynch syndrome, a genetic disorder caused by a mutation in DNA mismatch repair genes. The first study (Phase IB/II) is evaluating an off-the-shelf frameshift peptide vaccine, Nous-209, and the primary endpoints are immunogenicity and efficacy. The second study is a collaboration with two NCI Intramural Center for Immuno-Oncology investigators, Drs. James L. Gulley and Jeffrey Schlom, to use their adenoviral vaccines targeting tumor-associated antigens combined with an immune enhancer, an interleukin-15 superagonist, N-803. This N-308 study is the largest U.S. Lynch syndrome trial, and the primary endpoint is the cumulative incidence of colorectal neoplasms. Dr. Szabo explained that this is CP-CTNet's first cross-network study, which has had outstanding accrual.

The network consists of two major components: performance sites, which are directed by lead academic organizations (LAOs) along with affiliated organizations, and a Data Management, Auditing, and Statistical Center (DMASC). The CP-CTNet Steering Committee oversees the program. The scientific area of emphasis includes targeting the biology, developing strategies to optimize risk benefit, and repurposing drugs for prevention. Key program changes include switching the funding mechanism of the DMASC from a U24 to a UG1 to align with other NCI networks; setting aside restrictive funds for career development; increasing requirements for patient advocates, with funding for their work; increasing focus on quality of life and patient-reported outcomes; and developing supplemental programs. Regarding future scientific directions, several agents are in the pipeline within the PREVENT Cancer Preclinical Drug Development Program (PREVENT), including an inhaled bexarotene agent for lung cancer prevention, low-dose tamoxifen studies to optimize breast cancer prevention, and several vaccines.

A program evaluation was conducted in June 2023, and the external steering review panel recommended continuing the program with 6 years of funding and increased efforts on translational work. The panel recognized CP-CTNet as a unique program and the only one of its kind doing this research. They recommended increasing emphasis on mechanistic studies, funding more fellows, optimizing accrual and timelines, and utilizing research supplement funds. These recommendations have informed modifications to this program. A portfolio analysis of NCI investigator-initiated cancer prevention trials during this funding period identified 38 grants addressing early-phase clinical trials similar to CP-CTNet's 29 studies, but qualitative differences were found in the types of studies conducted. CP-CTNet focuses on premalignancy endpoints and in a larger range of target organs than those in the general portfolio, and it has the additional advantage of moving quickly from one study to another.

The objectives of this re-issue RFA are to continue to design and conduct early-phase clinical trials to assess the cancer-preventive potential of various interventions, characterize the effects of these agents on molecular targets and immune function, develop further scientific insights into the mechanism of cancer prevention, and facilitate the development and conduct of cross-network trials. CP-CTNet studies multiple organ sites and a broad range of interventions and clinical trial models, and it emphasizes risk benefit. NCI solicits studies and accepts unsolicited proposals from grantees. This re-issuance RFA will support the ongoing trials and CP-CTNet at full function, including additional performance sites, the DMASC and its activities, and LAOs (e.g., patient care costs). Dr. Szabo acknowledged and expressed appreciation to the CP-CTNet program grantees, DCP staff and contractors, collaborators, and participants in the early-phase prevention trials.

Subcommittee Review. Dr. Karen M. Basen-Engquist, Professor, Department of Health Disparities Research, Division of Cancer Prevention and Population Sciences, The University of Texas MD

Anderson Cancer Center, expressed the Subcommittee's enthusiasm and strong support for this re-issuance concept. Dr. Basen-Engquist conveyed that the Subcommittee recognizes this network as a critical infrastructure for advancing cancer prevention drugs through various interventions and the drug development pipeline. The Subcommittee noted the impressive new aspects of the concept, such as the inclusion of patient-reported outcomes for the later-phase trials, and appreciated NCI staff responses to their questions about mentoring, diverse recruitment, and inclusion of patient advocates.

In the discussion, the following points were made:

- The restricted funds for career development are intended to support one researcher per performance site and provide the principal investigator extra funds for services not typically covered, such as mentoring.

- NCI receives agents and matched placebos free of charge from pharmaceutical companies through established clinical trial agreements, but they do not directly contribute to the program's operational costs.

- NCI can use the reputation of CP-CTNet to convince pharmaceutical companies to participate in the program.

- Some principal investigators participating in CP-CTNet already have established relationships with colleagues in the pharmaceutical industry, and they leverage these resources.

- NCI identifies the agents for the studies and contacts pharmaceutical companies broadly. Generally, the smaller companies without the resources to support clinical trials agree to work with the CP-CTNet program.

- The ideas for drug agents used in the studies are identified through various paths, including an NCI internal group; the five LAOs and their affiliated organizations, which can consist of 80 to 90 clinical sites; other NCI programs (e.g., PREVENT); and the investigators submitting a proposal. The CP-CTNet Steering Committee evaluates agents identified in PREVENT and in proposals. NCI reviews the proposals.

- CP-CTNet conducts true (with healthy volunteers) Phase I studies, which can originate through the grant portfolio or the PREVENT program.

The first-year cost for the one-time issuance is estimated at $13.7 M for six UG1 awards, with a total cost of $83.3 M for 6 years.

Motion. A motion to concur on re-issuance of the DCP's RFA/Coop. Agr. entitled "Cancer Prevention Clinical Trials Network (CP-CTNet)" was approved with 19 ayes, 0 nays, and 1 abstention

Office of the Director
AIDS Malignancy Consortium (AMC) (Re-Issue RFA/Coop. Agr./Limited Competition)—
Dr. Mostafa Nokta

Dr. Mostafa Nokta, Director, AIDS Cancer Clinical Program, Office of HIV and AIDS Malignancy (OHAM), NCI, presented a re-issue concept for the AIDS Malignancy Consortium (AMC), an NCI-supported clinical trials group. Dr. Nokta reviewed the state of the HIV epidemic, which continues to be a worldwide public health problem. At the end of 2022, it was estimated that approximately 39 million people were living with HIV worldwide, and approximately 1.3 million new cases are being diagnosed annually. In terms of current cases, 1.2 million people in the United States; 25.6 million people in sub-

Saharan Africa; and 2.2. million people in Latin America live with HIV. Cancer has been a prominent manifestation of HIV/AIDS since the beginning of the epidemic and is a leading cause of morbidity and mortality among people with HIV.

People with HIV are at elevated risk of developing certain cancers. Non-Hodgkin's lymphoma, Kaposi sarcoma (KS), and cervical cancer were identified by the Centers for Disease Control and Prevention as AIDS-defining cancers. Non-AIDS-defining cancers include Hodgkin's lymphoma and lung, anal, liver, and head and neck cancers. More than two-thirds of people with HIV live in sub-Saharan Africa. Africa is also the epicenter of KS and other virus-related cancers, such as Burkitt lymphoma and cervical cancer. KS is the most common cancer among men in African countries. Cervical cancer is the second most common cancer among women in some countries in Africa.

The AMC was established in 1995, and its mission is to develop and evaluate clinical interventions for the treatment and prevention of malignancies in people with HIV; conduct Phase I, II, and III clinical trials of HIV-related malignancies; investigate the biology of HIV-related malignancies in clinical trials; and contribute specimens and clinical data to the AIDS and Cancer Specimen Resource. The AMC is composed of the Executive Committee, an administrative office, four disease working groups (Kaposi Sarcoma, Hematologic Malignancies, Solid Tumors, and Papillomavirus), a statistical office, an operations and data management office, and network core laboratories. The letters of intent and protocols are developed in the disease working groups and then reviewed by the Concept Review Committee and the Executive Committee before they are submitted to the Cancer Therapy Evaluation Program (CTEP) and NCI for final approval.

The AMC has 29 domestic clinical trial sites, 6 sites in sub-Saharan Africa, and 4 sites in Latin America. Dr. Nokta highlighted that the strengths of the AMC reside in the specialized clinical expertise of its investigators in studying and treating tumors in people with HIV. The AMC has been successful in recruiting diverse populations of patients, including underserved populations. The consortium provides people with HIV with needed access to clinical trials for cancer therapy. These patients often are marginalized and stigmatized and otherwise lack access to care.

In the current funding cycle, AMC investigators had 45 publications in peer-reviewed journals, developed 12 protocols, completed enrollment on 10 protocols, and accrued 1,422 patients into clinical trials; are actively accruing patients in 17 protocols. Approximately 63 percent of accrued U.S. participants are Black/African American or of Hispanic origin. The AMC patient population stratified by race and ethnicity shows that 50 percent of patients are Black/African American, 35 percent are Caucasian/White, 11 percent are Hispanic, and 1 percent are American Indian or Alaskan. To date, the largest AMC trial, Anal Cancer High-grade Squamous Intraepithelial Lesions [HSIL] Outcomes Research (commonly called ANCHOR) Study, has screened 10,885 participants and randomized 4,535 for treatment, with a 6-month follow-up.

Dr. Nokta highlighted numerous other AMC accomplishments since the last renewal. The consortium evaluated immunotherapy approaches to solid tumors; developed and assessed new approaches for frontline treatment of AIDS lymphoma and piloted the use of a chimeric antigen receptor T-cell therapeutic approach for treating refractory HIV-associated lymphoma; investigated treatments of novel mechanisms of action for KS; and evaluated the feasibility of treating ocular surface squamous neoplasia by surgical excision in sub-Saharan Africa. AMC investigators also assessed a therapeutic vaccine directly to HPV early genes (E6/E7) using electroporation; evaluated HPV vaccinations to reduce the recurrence of cervical HSIL after the loop electrosurgical excision procedure or cervical HSIL in women with HIV in sub-Saharan Africa; and trained a network of clinicians in high-resolution anoscopy to screen and treat anal HSIL in Latin American AMC sites. The team is currently assessing smoking cessation interventions in patients undergoing low-dose computerized tomography to the chest for lung cancer

screening.

In May 2023, the AMC program was evaluated by an external review team, which determined that the AMC is uniquely positioned to carry forward the NCI clinical agenda in HIV-associated malignancies. The evaluation also noted that AMC contributions had significantly impacted the field in the United States and globally, including seminal practice-changing contributions. The evaluators highlighted the value of the infrastructure developed by the ANCHOR trial, which they anticipate will further continue to grow the field. The AMC was commended for (1) the outstanding productivity of the disease working groups and the renewed focus on cutting-edge immunotherapy-based clinical trials, and (2) the significant and laudable efforts of the Career Enhancement Program and the development and capacity building of the international clinical sites. The evaluators proposed some recommendations, which the AMC began to address rapidly. They encouraged the AMC to form an external advisory board; increase the proportion of AMC studies being conducted in low- and middle-income countries (LMICs); continue to facilitate greater involvement of international junior investigators and trainees, especially those from Africa in AMC studies; and develop and convey plans to overcome obstacles to expanding novel therapies to international sites.

This re-issuance RFA will support ANCHOR correlative science, AMC Data Commons platform modifications, statistical data analysis and staff, new international clinical sites, logistical needs of the AMC and staff, and clinical care costs. NCI-appropriated AIDS funds, as established by the NIH Office of AIDS Research, will support this research.

Subcommittee Review. Dr. Nelson J. Chao, Donald D. and Elizabeth G. Cooke Professor, Chief, Division of Hematologic Malignancies and Cellular Therapy/BMT, Director, Global Cancer, Duke University School of Medicine, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Chao highlighted that the AMC has: 1) conducted practice-changing trials; 2) been able to build infrastructure in LMICs and increase training in those countries; and 3) created an environment within the clinical sites to treat other types of cancers.

In the discussion, the following points were made:

- The impact of HIV and AIDS in Africa and around the world remains a burden and may suggest the need for an upstream approach, such as prevention.

- Roughly 7 to 8 percent of NCI's AIDS appropriations support the AMC.

The first-year cost for the one-time issuance is estimated at $18 M for one UM1 award, with a total cost of $96.9 M for 6 years.

Motion. A motion to concur on the re-issuance of the OD's RFA/Coop. Agr./Limited Competition entitled "AIDS Malignancy Consortium (AMC)" was approved unanimously

VI. ONGOING AND NEW BUSINESS—DR. SHELTON EARP

Members suggested several agenda items for future meetings, including the following: an update on the Virtual Clinical Trial program and its impact on cancer care and prevention; an update on workforce training and the role of the Cancer Centers; a report on the Cancer Grand Challenges program and AI-focused challenges; a report on NCI investments in integrating AI and data science in cancer research and a review of NCI's programmatic efforts to use AI to accelerate cancer research; a review of leveraging data sets and implementing new data sharing approaches; and a progress report on the Cancer Moonshot. BSA members were asked to forward additional suggestions to Drs. Earp and Gray.

VII. ADJOURNMENT—DR. SHELTON EARP

There being no further business, the 8th virtual meeting of the BSA was adjourned at 4:47 p.m. on Wednesday, 20 March 2024.

Date	Shelton Earp, M.D. Chair, Board of Scientific Advisors
Date	Paulette S. Gray, Ph.D. Executive Secretary, Board of Scientific Advisors