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

6th Virtual Meeting of the BOARD OF SCIENTIFIC ADVISORS

Summary of Meeting

March 28–29, 2022

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
28–29 March 2022

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 6th virtual regular meeting on Monday, 28 March 2022, at 1:00 p.m. Dr. Keith T. Flaherty, Director, Clinical Research, Massachusetts General Hospital Cancer Center, presided as Chair. The meeting was open to the public on Monday, 28 March 2022, from 1:00 p.m. until 5:20 p.m. and on Tuesday, 29 March 2022, from 1:00 p.m. until 2:47 p.m. for the consideration of new requests for applications (RFAs), Cooperative Agreements (Coop. Agr.), requests for proposals (RFPs), and program announcements with special receipt, referral, and/or review (PARs) of new and re-issue concepts presented by NCI Program staff.

BSA Board Members Present

Dr. Keith T. Flaherty (Chair)
Dr. Chandraknath Are
Dr. Suzanne J. Baker
Dr. Karen M. Basen-Engquist
Dr. Michael John Becich
Dr. Mary C. Beckerle
Dr. Melissa L. Bondy
Dr. Otis W. Brawley
Dr. Andrew T. Chan
Dr. Nelson J. Chao
Dr. Gloria D. Coronado
Dr. Chyke A. Doubeni
Dr. Shelton Earp
Dr. Jennifer R. Grandis
Dr. Dorothy K. Hatsukami
Dr. Trey Ideker
Dr. Karen E. Knudsen
Dr. Michelle M. Le Beau
Dr. Karen M. Mustian
Dr. Sylvia Katina Plevritis
Dr. W. Kimryn Rathmell
Dr. Erle S. Robertson
Dr. Leslie L. Robison
Dr. Robert D. Schreiber
Dr. David Sidransky
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson
Dr. Robert H. Vonderheide

Board Members Absent

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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MONDAY, 28 MARCH 2022

I. CALL TO ORDER AND OPENING REMARKS— DR. KEITH T. FLAHERTY

Dr. Flaherty called to order the 6th 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. Flaherty 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 (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

Dr. Flaherty called attention to future meeting dates contained in the agenda. He noted that the next BSA meeting will be a joint meeting with the National Cancer Advisory Board (NCAB), scheduled for 13–15 June 2022, and will be virtual.

II. NCI DIRECTOR'S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman E. Sharpless, Director, NCI, also welcomed BSA members and attendees to the 6th virtual meeting of the BSA. He provided updates on the NCI budget and appropriations, the Cancer Moonshot℠, efforts to promote health equity, and research progress across NCI programs and initiatives.

NCI Budget and Appropriations. Dr. Sharpless reported that the fiscal year (FY) 2022 Omnibus appropriations bill was approved in March 2022. He remarked that bipartisan support from Congress for biomedical science and cancer research remains strong. NCI appropriations for FY 2022 include $6.9 billion (B) for the NCI, which is a $353 million (M) increase above the FY 2021 enacted budget; $194 M for the 21st Century Cures Act, specifically the Cancer Moonshot℠ 1.0 component, which is set to end in FY 2023; and $50 M for the Childhood Cancer Data Initiative (CCDI). A one-time supplemental appropriation within the Paycheck Protection Program and Health Care Enhancement Act of 2020 was provided in April 2020 for COVID-19 serology studies. U.S. Department of Health and Human Services (HHS) appropriations for FY 2022 include $1 B for Advanced Research Projects Agency for Health (ARPA-H). Research funding for this new initiative that will focus on a variety of diseases (including cancer), has been appropriated for 3 years beginning in FY 2022 and ending in FY 2024. Secretary Xavier Becerra has been authorized to transfer funds 30 days after the approval and currently is deciding, administratively, on a location for ARPA-H, either as part of the NIH or elsewhere within HHS. The authorizing legislation that will provide details on the authorities and flexibilities of this initiative is still pending.

Dr. Sharpless reminded the BSA that the NCI has been increasing paylines significantly over the past 2 years and explained that out-year costs for those grants will need to be incurred in FY 2022. This requires the NCI to make different decisions regarding the funding structure and policy for Research Project Grant (RPG) awards for FY 2022. The paylines for competing awards for FY 2022 will be as follows: 11th percentile for R01 grants to established and new investigators, 16th percentile for R01 grants to early-stage investigators (ESIs), and 9th percentile for R21 exploratory grants. There will be a 2 percent decrease in funding non-competing awards in the RPG pool, except for most ESI awards, NCI-Designated Cancer Centers (Cancer Centers) Support Grants (CCSGs), Small Business Innovation Research (SBIR)/ Small Business Technology Transfer (STTR) awards, and training grants. Dr. Sharpless explained that there will be a 2 percent across-the-board reduction in funding for NCI Divisions, Offices, and Centers; operating costs will not be affected. The final policy details will be published on the NCI website. Further details on the NCI appropriations will be provided later in the meeting.

Dr. Sharpless called attention to two opinion columns advocating increased funding for the NCI. In the 28 December 2021 issue of *Scientific American*, Senators Chris Coons (D-Delaware) and Jerry Moran

(R-Kansas) proposed a robust, sustained investment of $1 B to the NCI to make progress in cancer research, particularly in extramural funding. Additionally, in the 17 February 2022 issue of *The Hill*, Dr. Caryn Lerman, President, Association of American Cancer Institutes (AACI), and Dr. Robert A. Winn, Vice President and President-Elect, AACI, advocated funding cancer research. They cited data indicating that the cost of cancer in the United States is projected to exceed $245 B by 2030. Dr. Sharpless conveyed that the FY 2022 budget increase and that the vote of support from Congress reflects the work of advocacy in the community, including this Board.

Cancer Moonshot℠ Update and White House Announcements. Dr. Sharpless informed the BSA that on 2 February 2022, President Joseph R. Biden announced his plans to reignite the Cancer Moonshot℠, beginning the Cancer Moonshot℠ 2.0. In his speech, President Biden stated that fighting cancer was a top priority for his Administration, and he expressed strong support for the initiative and announced several new goals for "Ending cancer as we know it." Dr. Sharpless stated that President Biden announced a new White House goal to reduce the death rate from cancer by 50 percent during the next 25 years, a reduction of age-adjusted mortality from 146 to 73 deaths per 100,000. This goal will require a focus on prevention, screening, therapies, tobacco control, and health disparities. Dr. Sharpless reiterated that this goal is ambitious but feasible, given that the age-adjusted cancer mortality has declined significantly over the past decade. In addition, the NCI has discussed internally, and with colleagues at the White House, efforts aimed at "Ending cancer as we know it" and has put forth seven areas to advance progress. These can be summarized as (1) diagnose cancer sooner; (2) prevent cancer; (3) address inequities; (4) target treatments to the right patients; (5) speed progress against the most deadly and rare cancers, including childhood cancers; (6) support patients, caregivers, and survivors; and (7) learn from all patients. The Cancer Moonshot℠ 2.0 aligns with these goals that reflect the scale and scope of how this effort is envisioned, as well as the directions understood to be important and promising. The goals of "Ending cancer as we know it" are framed differently from the traditional approach (e.g., targeting cancer-related genes or elucidating the immune response). The aim is to intentionally observe what cancer is today, how patients experience it, and how this tragic diagnosis that affects the daily lives of many patients can be improved.

A major focus of the Cancer Moonshot℠ 2.0 is on prevention, screening, and early detection, which are important tools to control cancer at the population health level. Dr. Sharpless noted that the NCI began modeling trends related to cancer screening and care early in the pandemic. The President's Cancer Panel recently released a report, *Closing Gaps in Cancer Screening: Connecting People, Communities, and Systems to Improve Equity and Access*. Barriers identified in the report included lack of knowledge of guidelines and provider recommendations, fears or concerns about medical procedures, and difficulty navigating the health system. Community-oriented outreach is needed to address these barriers. Dr. Sharpless reiterated that cancer screenings have declined during the COVID-19 pandemic and have not recovered fully. President Biden emphasized the need to ensure that everyone in the United States benefits equitably from screening capabilities (e.g., at-home screening, mobile screening, community health networks) and called for an all-government approach to address this problem. The NCI continues to pursue efforts in this area (e.g., through Cancer Centers) to ensure that cancer screening is made clear as a national priority. The NCI also will collect qualitative and quantitative data to understand these needs and work in partnership with the CDC, CMS, and Health Resources and Services Administration (HRSA) on this topic. First Lady Dr. Jill Biden has been an important partner in advocating on this topic.

Dr. Sharpless informed the BSA that in February 2022, President Biden named temporary leadership to fill the recent vacancy in the White House Office of Science and Technology Policy (OSTP); Dr. Alondra Nelson will perform the duties of the OSTP Director, and Dr. Francis S. Collins will perform the duties of Science Advisor to the President and Co-Chair of the President's Council of Advisors on Science and Technology.

In his announcement, President Biden detailed his Administration's broader and more ambitious set of goals and priorities for ending cancer that extends beyond any one Agency or Office. He described an all-government approach, which includes convening a Cancer Cabinet. The first Cancer Cabinet meeting was held on 16 March 2022 and brought together several Agencies, Departments, and Offices. These included the NCI; U.S. Departments of Veterans Affairs (VA), Defense (DoD), Energy (DOE), and Agriculture (USDA); U.S. Environmental Protection Agency (EPA); U.S. Food and Drug Administration (FDA); Centers for Medicare & Medicaid Services (CMS); Centers for Disease Control and Prevention (CDC); HHS; and OSTP. The NCI will be responsible primarily for the research aspects of this effort (e.g., new treatments, better prevention). Other aspects will include increasing access to care, improving how care is delivered within communities, and promoting health equity.

BSA members were reminded that the success of the initial Cancer Moonshot℠, which was launched in 2016 and has been led by Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development, NCI, was a major contributing factor to NCI's progress during the past 5 years. Dr. Sharpless stated that the Cancer Moonshot℠ remains a work in progress. The initiative has three ambitious goals: (1) Accelerate scientific discovery in cancer, (2) foster greater collaboration, and (3) improve data sharing. The Cancer Moonshot℠ has led to more than 70 consortia or programs and more than 240 new research projects. Drs. Sharpless and Singer recently published a review on Cancer Moonshot℠ outcomes. Cancer Moonshot℠ 1.0 is set to end in FY 2023 and the Administration's reigniting this initiative provides an opportune time to discuss what would be the next era.

Promoting Health Equity. Dr. Sharpless emphasized that a large component of ending cancer and achieving the Administration's goals for cancer mortality involves addressing health equity. President Biden emphasized that progress in cancer benefits all Americans. Health inequities in the United States are reflected in the mortality rates and are influenced by poverty. CDC 4-year reports from 2000 to 2019 show that the age-adjusted mortality rates were higher in non-Hispanic Black/African American patients with cancer than in other minority patients, and this disparity is observed geographically. Although improvements have been made over the years, striking differences and heterogeneity among non-Hispanic American Indians/Alaska Natives persist, and geographic differences also have been observed.

One approach to changing the experience of cancer for patients is examining the prism of cancer mortality, particularly age-adjusted cancer mortality across the United States. From 2005 to 2019, the age-adjusted cancer mortality declined significantly. Heterogeneity across the states, however, was pronounced and persists today. Geography remains a significant factor in cancer mortality, reflecting such factors as race, poverty, and access to care. The NCI is responsible for understanding the underlying causes of these disparities. Understanding cancer disparities is complicated and requires thoughtful use of data and consideration of multiple facets and aspects of this problem. The NCI has long been focused on reducing disparities and is working toward that goal.

The NCI also is addressing the need to have a continuous flow of talent through the research career pipeline. The NCI Equity and Inclusion Program, overseen by the NCI Equity Council, launched the Early Investigator Advancement Program (EIAP) for the advancement of scientists from diverse backgrounds. The first cohort of ESIs and new investigators, consisting of more than 20 scholars from across the Cancer Centers and 16 universities, soon will initiate. The aim is to submit R01 applications in fall 2022. The NCI is working with the NIH to administer the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program, which is a Common Fund initiative that supports institutions in recruiting diverse cohorts of faculty and implementing a sustained culture of inclusive excellence. The initial cohort awardees will be announced soon. In February 2021, the NCI released a notice of special interest inviting applications to support administrative supplements to existing awards of scientists who are outstanding mentors and to enhance diversity, inclusion, equity, and accessibility in biomedical research. Applications are due 7 April 2022. The NCI Equity and Inclusion Program also

introduced the Connecting Underrepresented Populations to Clinical Trials (CUSP2CT) concept in 2021, which the BSA approved. Projects will address key issues that affect diversity in clinical trials and will improve the dissemination of information and care into underserved communities. Applications were due on the date of this meeting, 28 March 2022.

NCI Programs and Initiatives. Dr. Sharpless provided updates on cancer research progress across NCI programs and initiatives. He highlighted two recent publications posted to NCI Bottom Line: A Blog about Grants and More. An article posted on 25 March 2022 describes ways the NCI has worked to reduce the administrative burden on cancer researchers regarding annual grant renewals and competing resubmissions. One major approach has been to extend the period of grant awards by, for example, extending 5-year grants to 7-year grants for ESIs, outstanding investigators, and CCSGs. The NCI also is aiming to demystify the process of submitting a grant by sponsoring educational opportunities and webinars and promoting communication among NCI program officers and managers. A second article posted on 17 February 2022 addresses modular versus non-modular budgets, a topic of interest among junior scientists working at the Cancer Centers.

Division of Cancer Control and Population Sciences (DCCPS) Investigator Dr. Jennifer M. Croswell and extramural authors reported findings of a large multicenter study of individuals screened for lung cancer in a trial conducted by the Population-based Research to Optimize the Screening Process (PROSPR) consortium. The study showed that adherence to both annual lung cancer screening and recommended follow-up was greater at centralized screening programs. Racial disparities were higher at decentralized lung cancer screening programs.

DCCPS and Division of Cancer Epidemiology and Genetics (DCEG) investigators collaborated with the CDC on a study addressing the potential public health benefits of changing daily physical activity routines. The National Health and Nutrition Examination Survey (NHANES) data were used in this study. The results reported in the 24 January 2022 issue of the *Journal of the American Medical Association Internal Medicine* demonstrated that a small increase in physical activity could avert 7 to 17 percent of deaths per year. This NHANES study, which examined 4,800 U.S. adults, is the first to estimate preventable deaths through physical activity using accelerometer-based measurements in this population. Although the study design limitations of 1 week of monitoring will not infer causality, these data present actionable results that the NCI can evaluate further with additional research. Lack of physical activity partly affects obesity, a growing problem in the United States, and has become one of the leading modifiable behaviors affecting cancer risk. Increased physical activity may play a role in reducing the mortality of obesity-associated cancers at the population level.

Data generated by the Serological Sciences Network for COVID-19 (SeroNet) are being reported. A new DCCPS-supported extramural study led by The Ohio State University demonstrated that neutralizing antibody responses elicited by SARS-CoV-2 mRNA vaccination wane over time and are boosted by breakthrough infection. In fact, people who received two doses of Pfizer or Moderna vaccines did generate virus-neutralizing antibodies, but antibody levels dropped considerably over 6 months, suggesting declining immunity over time. Participants had much-reduced protection against newer SARS-CoV-2 variants, including Delta and Omicron; these findings are consistent with earlier studies that showed a significant decline in neutralizing antibodies against Omicron in people who received two shots, with improved neutralizing ability after a booster.

Emerging technologies have enabled the development of blood-based multi-cancer detection (MCED) tests, which can detect multiple cancers simultaneously in otherwise healthy individuals. This high-sensitivity and high-specificity test for multiple cancers would require further diagnostic studies in the event of a positive MCED result. More than 20 MCED tests are in development presently. Dr. Sharpless remarked that these developments are exciting and could have a significant impact on cancer detection at

the population level if the screening is applied robustly. He cautioned, however, that screening and early detection can incur the potential for overdiagnosis and overtreatment; thus, appropriate clinical trials are needed to understand the benefits of these technologies. Federal agencies led by NCI will develop a focused program to study and evaluate MCED tests expeditiously. The NCI published a request for information (RFI) seeking input from the community on this topic, and responses are being reviewed.

The CCDI component, Childhood Molecular Characterization Protocol, which builds on Project:EveryChild, launched on 21 March 2022. The Protocol is open to all children with cancer, regardless of treatment facility or location. The aim is to gather clinical and molecular information from every child with cancer, with the goal of characterizing approximately 3,000 children with hard-to-treat cancers. The NCI will support the sequencing analysis to be performed by a Clinical Laboratory Improvement Amendments (CLIA)–accredited laboratory. The Children's Oncology Group (COG) and Biopathology Center at Abigail Wexner Research Institute at Nationwide Children's Hospital will be responsible for specimen handling.

NCI New Personnel Announcement. Dr. Sharpless stated that the NCI has long been committed to unraveling the intricacies of childhood cancer, recognizing that treatment is different for children than adults. The CCDI has demonstrated unique opportunities and challenges in this area. In particular, more efforts related to data aggregation are needed. The NCI recently announced that Dr. Brigitte C. Widemann, Chief, Pediatric Oncology Branch, CCR, NCI, has been appointed as Special Advisor to the Director for Childhood Cancer. Dr. Sharpless remarked that Dr. Widemann has extensive experience in this area, and the NCI looks forward to her support.

Progress and Future of Cancer Research. Summarizing the 2 February 2022 White House event, Dr. Sharpless explained the First Lady's perception of cancer research reflected in her speech, in which she noted this time as being a golden age of cancer research and emphasized the need to make progress against cancer. The Administration believes now is the time to make progress and succeed. Dr. Sharpless next reflected on his career as an oncology fellow working with well-known cancer leader Dr. Thomas J. Lynch, Jr., and treating patients in the 1990s who had incurable metastatic lung cancer. Advances have led to curative therapies for people with metastatic lung cancer. He noted being an optimist as an oncologist to provide hope to patients with cancer. The main source of that optimism, Dr. Sharpless explained, lies in the people involved in planning various cancer-related initiatives—in and outside of the government—who are devoted to improving the lives of people with cancer and continuing to make progress in cancer research.

In the discussion, the following points were made:

- The diagnosis of prostate cancer for the first time is shifting to a more advanced stage of disease, indicating that the screening efforts should be prioritized.

- Dr. Sharpless called attention to the declining mortality rate in prostate cancer relative to prostate-specific antigen (PSA) screening, noting that the NCI and American Urological Association are monitoring these trends. He added that advice is needed from the extramural community about next steps in PSA screening. Potential scientific opportunities include combining PSA screening with other technologies (e.g., imaging or risk scoring). The U.S. Preventive Services Task Force recommendation is that individuals discuss screening with their doctors.

- The field can consider incorporating genetics of risk, raising awareness of current screening guidelines, and promoting the uptake of evidence-based screening efforts

III. A PERSPECTIVE ON THE FY 2022 NCI BUDGET APPROPRIATION—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, presented on the FY 2022 paylines, RPG pool and trends, and budget decisions. He expressed appreciation to NCI Office of Budget and Finance, Office of Scientific Operations, Center for Research Strategy, and Office of Communications and Public Liaison for their support in generating these data. The RPG pool is the largest investment of NCI funding, at 43 percent of the total budget. Non-RPG activities include the Cancer Centers, Specialized Programs of Research Excellence (SPOREs), and training. Of the 43 percent of RPG pool funding, 56 percent supports traditional R01 grants, an additional 3 percent funds R01 RFAs, and the remainder supports other mechanisms, such as Outstanding Investigator Awards and SBIR/STTR awards. From FY 2018 to the current fiscal year, the NCI appropriation increased $1.05 B and, with prioritization, the RPG budget was increased from 41 percent to 44 percent.

From FY 2018 to FY 2021, the NCI increased paylines for ESI R01/R37 from the 12th to 16th percentile and funded 134 awards in FY 2021. For established investigators, the payline was at the 10th percentile in FY 2016, decreased to the 8th percentile in FY 2019, and returned to the 11th percentile in FY 2021. A total of 811 awards was funded in FY 2021. The increases in the NCI budget and the prioritization substantially increased the total number of ESI and established investigator awards in FY 2021 compared with previous years.

Dr. Lowy reminded BSA members that almost all RPG awards are multiyear awards, with an average duration of 5 years. The NCI generally funds only the first year in the fiscal year the awards are made to prioritize funding competing awards. With the proposed FY 2022 paylines, approximately 52 percent of the increase in the NCI FY 2022 appropriation will be invested in the RPG pool. Each year, two overall investment categories make up the RPG pool: competing awards and non-competing awards. For established investigators, most awards completed in FY 2021 initially were awarded in FY 2017.

Two main sources comprise the funding for competing and non-competing RPG awards. These include turnover of funds from non-competing RPG awards completed in the prior year and the addition of funds from the NCI appropriation, if turnover dollars are insufficient. The dollars derived from completed awards are usually lower than what is needed. Several factors account for this discrepancy. For competing awards, the number of completed awards will be smaller than the number of competing awards, and the average cost of each competing award will be higher than average cost of each completed award. For non-competing awards, each year, the total number of awards and average amount of each award will usually be higher than in the previous year.

Dr. Lowy described the option of funding non-competing RPG awards at less than the 100 percent of commitment level. The NCI considers this option only when funds from 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 non-competing grants at 100 percent commitment. The NCI typically prioritizes funding additional competing awards.

In the discussion, the following points were made:

- The option to fund non-competing RPG awards at less than the 100 percent of commitment level is a decision for FY 2022. Funding levels will automatically be restored in FY 2023 unless the scenario is similar.

- Although the budgets across the extramural and intramural Divisions are reduced in FY 2022, the NCI anticipates utilizing the "fund by exception option"; the precise percentage remains to be determined.

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

Ms. M.K. Holohan, Director, Office of Government and Congressional Relations, reported on the FY 2022 and 2023 appropriations, COVID-19 funding, and legislation and issues to monitor. The FY 2022 Omnibus Appropriations Act was enacted on 15 March 2022, and includes a $353 M increase for the NCI. Ms. Holohan said that the FY 2022 ends in 187 days from this meeting, and reminded the BSA members that negotiations on the bipartisan infrastructure bill, FY 2022 budget resolution, and Build Back Better (BBB) package had diverted legislators' attention from the regular appropriations work. With the release of the President's FY 2023 budget request on 28 March 2022, budget hearings for executive branch officers to present their budgets will commence. The Director of the Office of Management and Budget, Shalanda Young, will testify to the House and Senate Budget Committee this week. HHS Secretary Becerra will testify before the House appropriators on 31 March 2022 to present the HHS part of the budget request.

Ms. Holohan noted that the FY 2022 appropriations, after 11 years, returned congressional earmarks on House appropriation bills to support Community Project Funding requests in the House and Congressionally Directed Spending requests in the Senate. More than 4,000 requests for funding have been submitted. She echoed Dr. Sharpless on the FY 2022 Omnibus appropriation of $1 B for ARPA-H directed to the HHS, but authoring legislation is still pending. Two bills introduced in the House and a proposal in the Senate will be developed in tandem and will address authorizing legislation for ARPA-H.

Telehealth is one area receiving increased attention in Congress. More than 50 bills have been introduced during this 117th Congress. The main issues and concerns facing telehealth provisions are retaining the flexibility favored by patients and providers, while balancing payments and problems with fraud and fitting this health care area into the existing system. The Creating Opportunities Now for Necessary and Effective Care Technologies (CONNECT) for Health Act is one of the bills receiving the most support, with 61 bipartisan co-sponsors in the Senate and 124 in the House. CONNECT aims to permanently remove geographic restrictions on telehealth services. The FY 2022 Omnibus extends Medicare telehealth flexibilities for 151 days past the end of the COVID-19 public health emergency, but does not make these changes permanent. The NCI is monitoring these concerns and new legislation closely.

Regarding American competitiveness legislation, on 8 June 2021, the Senate passed the U.S. Innovation and Competition Act (USICA). The main focus of USICA is on competitiveness with China and includes increases to the National Science Foundation; DOE, National Aeronautics and Space Administration, and U.S. Department of Commerce, as well as support for the U.S. semiconductor industry. This Act also doubles the Defense Advanced Research Projects Agency (DARPA) budget over a 5-year period and includes funding provisions for NIH. On 4 February 2022, the House passed similar legislation, the America Creating Opportunities for Manufacturing, Pre-Eminence in Technology, and Economic Strength (COMPETES) Act of 2022. COMPETES reauthorizes the SBIR/STTR program through FY 2027; supports low-dose radiation research at the DOE; boosts U.S. competitiveness in the semiconductor industry; and has provisions for climate research. The initial cloture vote was held on 23 March 2022, the next Senate vote is scheduled for the date of this meeting, 28 March 2022, and the overall conference package is to be determined.

Ms. Holohan informed the BSA that several members of Congress have announced their retirement. As of 25 January 2022, six Senators (1 Democrat and 5 Republicans) and 48 Representatives (31 Democrats and 17 Republicans) will be retiring. Ms. Holohan acknowledged Representatives who have been

engaged with or had leadership roles affecting the NCI and NIH during their tenures.

In the discussion, the following point was made:

- Regarding the scope of the proposed bills concerning ARPA-H, Representatives Diana DeGette (D-Colorado) and Frederick Stephen Upton (R-Michigan) introduced a draft version of the 21st Century Cures Act 2.0 to the House in November 2021. Cures 2.0 would establish ARPA-H within the NIH and authorize research funding in several areas, including telehealth. Representative Anna Eshoo (D-California), Chair, Health Subcommittee of the House Committee on Energy and Commerce, introduced a bill to establish ARPA-H within HHS. In January 2022, the Senate Committee on Health Education, Labor and Pensions, chaired by Senator Patty Murray (D-Washington), released the draft version of the Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics (PREVENT Pandemics) Act to establish ARPA-H within the NIH.

V. RFA/COOP. AGR./RFP and PAR CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

Division of Cancer Prevention

Precompetitive Collaboration on Liquid Biopsy for Early Cancer Assessment (Re-Issue RFA/Coop. Agr.)—Dr. Lynn Sobara

Dr. Lynn Sobara, Program Director, Division of Cancer Prevention (DCP), NCI, presented a re-issue RFA concept for the precompetitive collaboration on liquid biopsy for early cancer assessment. The Consortium (or Liver Biopsy Consortium [LBC]) was established in 2018 to address the challenges impeding the progress in implementing liquid biopsy technologies for early cancer detection. Although substantial progress has been made toward developing technologies and associated adaptability toward clinical use since inception of this concept, several gaps remain. These include low levels of genetic targets, challenges regarding cancer biology and screening, and concerns related to data sharing and verification. A December 2021 external review committee program evaluation concluded that the innovative structure of the program, combined with the success of the partnership teams, has resulted in significant advances in developing needed tests for early cancer detection and longitudinal assessment of treatment response. All four reviewers strongly recommended continued funding for the LBC. The current program consists of six teams composed of academic and industrial partners, a steering committee, and two working groups: Study Design and Biospecimen. The six teams, which are developing or refining technologies and assays for early cancer assessment, are evaluating model systems of lung, ovary, breast, and glioblastoma cancers. In addition, set-aside funds support collaborative projects both within and external to the LBC, and interlaboratory studies are ongoing.

Regarding major accomplishments and scientific advances, the Consortium collectively has had 42 publications and has developed several assays and model systems. Each team has addressed issues that impede liquid biopsy technologies from advancing into the early detection space, such as lowering the sample volume, reducing background noise, increasing sensitivity and the limit of detection, and utilizing biological fluids (biofluids) other than blood. Dr. Sobara highlighted one example of the program's technologies. The Electric Field-Induced Release and Measurement (EFIRM) technology was developed by the University of California, Los Angeles–EZLife Bio Inc. partnership. The EFRIM platform uses 40–100 microliters of saliva or plasma to detect somatic mutations in circulating-free DNA for early lung cancer detection. This system uniquely detects mutant single-stranded DNA, with no sample processing or extraction in a 1.5 hour capture-reporter probe process that has high specificity, accuracy, and sensitivity. The EFRIM technology was validated in a pilot study of a series of patient samples. This platform can be multiplexed, is biofluid agnostic, is now CLIA-certified, and is currently undergoing

further validation by the National Institutes of Standards and Technology.

The re-issue RFA will support the LBC to expand the capacity of new liquid biopsy technologies, assays, and methods to enable more accurate assessment of low variant allele frequency; validate current and new technologies and assays in different biofluids, particularly in patients with early-stage disease or those at high-risk for cancer; include untargeted and targeted identification of protein-based analytes for liquid biopsy panels; and develop algorithms for tissue of origin determinations. In addition, this re-issue concept will establish a Data Management and Coordinating Unit (DMCU), responding to the recommendation of the external review committee. A portfolio analysis of the NIH-wide and the NCI-focused grants addressing liquid biopsy technology development revealed a $24 M investment for FY 2020 and FY 2021 combined. Of the $24 M investments, the NCI awarded 42 grants amounting to $10 M, which included the LBC. The NCI DCP anticipates building on the established public–private partnership infrastructure to address the remaining gaps in research and challenges.

Subcommittee Review. Dr. Erle Robertson, Harry P. Schenk Endowed Chair, Professor, Vice-Chair, Department of Otorhinolaryngology, University of Pennsylvania School of Medicine, expressed the Subcommittee's enthusiasm and support for the re-issue concept. Dr. Robertson conveyed the Subcommittee's appreciation to the NCI staff for responding to their questions on validating findings, fostering and maintaining collaborations, and detailing the set-aside budget efforts.

In the discussion, the following points were made:

- The LBC primarily focuses on new technologies it developed at this phase of the program, but it can consider leveraging existing technologies (e.g., Grail, Thrive) for validating and testing. In fact, the Consortium is all inclusive and complements but does not compete with existing technologies. The aim is to encourage data and technology sharing, as well as assay and model verification among the major stakeholders in the liquid biopsy field, with the goal to embrace technologies that potentially could be used in the future.

- Although the details of the ARPA-H mandate are pending, the Administration has encouraged that cancer be among the diseases of focus, but this will be up to the future director of that agency, once named. The NCI DCP has plans to conduct clinical trials using the technologies developed in the LBC and will work broadly with ARPA-H leadership toward a common goal.

- The LBC should ensure adequate focus on the development of computational and artificial intelligence and machine learning tools for data analysis within the broader activities of the DMCU.

- The LBC should plan and conduct the necessary basic science regarding the use of novel liquid biopsy technologies for early cancer detection, including the EFRIM platform.

- The NCI can examine the feasibility of investments within the NCI Intramural Research Program regarding novel liquid biopsy technologies.

The first-year cost for the one-time issuance is estimated at $6.7 M for six U01 awards and one U24 award, with a total cost of $33.5 M for 5 years.

Motion. A motion to concur on the re-issuance of the DCP's RFA/Coop. Agr. entitled "Precompetitive Collaboration on Liquid Biopsy for Early Cancer Assessment" was approved with 25 ayes, zero nays, and 1 abstention.

Consortium on Translational Research in Early Detection of Liver Cancer (TLC) (Re-Issue RFA/Coop. Agr.)—Dr. JoAnn S. Rinaudo

Dr. JoAnn S. Rinaudo, Program Director, DCP, NCI, presented a re-issue RFA concept to continue the translational liver cancer (TLC) Consortium. Established in 2018, the TLC aims to advance research on the early detection of liver cancer. The TLC fits with the recommendations of the Senate Committee on Appropriations that the NCI continue to support liver cancer research across the research portfolio and that the Federal Implementation Plan for Viral Hepatitis continue to support the early detection of liver cancer.

The current TLC organizational structure is composed of five Translational Research Centers (i.e., clinical sites); a TLC Steering Committee; a data and coordinating center; and four working groups: Common Data Elements and Harmonization, Biomarkers and Imaging, Documents, and Early Career. An external evaluation of the TLC in December 2021 detailed two important conclusions about the progress of the program in the final report. First, the direction of the TLC remains tremendously relevant because of the increasing incidence of liver cancers, particularly hepatocellular carcinoma (HCC) in the United States. Second, the Consortium connects outstanding investigators who are achieving goals that would be difficult to attain elsewhere. The external evaluation panel outlined the following future directions and recommendations for the TLC: (1) Expand and support Phase III biomarker studies, (2) expand cohorts and ensure racial and ethnic diversity, (3) foster additional partnerships and collaborations, (4) encourage additional trans-TLC studies, and (5) increase TLC resources and funding.

Since its inception, the TLC has had several major accomplishments across research studies resulting in 24 publications. In the area of risk assessment, investigators developed and validated a prognostic liver secretome signature to determine HCC risk and developed a polygenic risk score (PRS) using a large multiethnic cohort of patients with cirrhosis. A higher PRS is associated with a higher risk of HCC. In the area of improved surveillance, the TLC developed and implemented an electronic medical record best practice advisory for the surveillance of HCC, which currently is being evaluated. In addition, investigators evaluated an abbreviated magnetic resonance imaging technique for HCC and found this method more accurate than ultrasound in detecting early-stage disease. In terms of early detection of HCC, the Consortium developed a novel cell-free DNA methylome sequencing assay, which differentiated liver cancer from cirrhosis in early pre-validation studies. Another team of TLC investigators evaluated proteomic profiles and found a decrease in TGF-β receptor subunit 2 in samples of patients with HCC samples, but to a lesser extent in patients with cirrhosis.

Regarding future directions, a consortium-wide collaborative project will address a major unmet need to differentiate benign from malignant indeterminate nodules, categorized as Liver Imaging Reporting and Data System (LI-RADS(3 and LI-RADS 4 lesions found in approximately 20 percent of the patients undergoing HCC screening. The goals are to develop a retrospective and prospective study of LR3/4 nodules in cirrhosis patients using a combination of clinical blood-based and imaging biomarkers. A recent portfolio analysis showed that in FY 2020, the NCI invested $130 M in liver cancer research, of which the majority supported research on tumor biology, with only $6 M of funding focusing on early detection or surveillance.

This re-issue concept will support continued efforts of the TLC to conduct risk assessment, improved surveillance, and early detection of HCC studies. The RFA also will support expanding the virtual repository, building future cohorts, and assembling a pool of experienced and accomplished liver cancer investigators.

Subcommittee Review. Dr. Andrew T. Chan, Chief, Clinical and Translational Epidemiology Unit, Massachusetts General Hospital (MGH), Director of Epidemiology, MGH Cancer Center, Daniel K. Podolsky Professor of Medicine, Harvard Medical School, expressed the Subcommittee's enthusiasm and

support for the re-issue concept. Dr. Chan highlighted strengths and attributes of the program that include addressing an unmet need of liver cancer translational science; leading an initial group of liver cancer investigators; developing a collaborative infrastructure; establishing a virtual biorepository of diverse representation; and advancing existing NCI initiatives (e.g., the Early Detection Research Network). The Subcommittee noted that establishing and maturing new clinical cohorts and gaining new insights from the TLC collaborative efforts necessitate continuing the program.

In the discussion, the following point was made:

- From a liver and pancreas cancer and cancer surgery perspective, this program is timely to potentially provide insight into the rising incidence of nonalcoholic steatohepatitis and nonalcoholic fatty liver disease, particularly in patients who are not obese, which has been a major risk factor for these conditions.

The first-year cost for the one-time issuance is estimated at $5 M for five U01 awards and one U24 award, with a total cost of $25 M for 5 years.

Motion. A motion to concur on the re-issuance of the DCP's RFA/Coop. Agr. entitled "Consortium on Translational Research in Early Detection of Liver Cancer (TLC)" was approved with 25 ayes, zero nays, and 1 abstention.

VI. STEM CELL SIGNALS IN CANCER HETEROGENEITY AND THERAPY RESISTANCE—DR. TANNISHTHA REYA

Dr. Sharpless introduced Dr. Tannishtha Reya, Professor, Department of Pharmacology, Director, Division of Cancer Biology, University of California, San Diego, School of Medicine, who is a recipient of an NCI Outstanding Investigator Award.

Dr. Reya presented on the role of stem cell signals in the origin, progression, and therapy resistance in cancer. Dr. Reya explained that her research is focused on the reduced stem cell differentiation that is associated with malignant lesions. The Reya laboratory has the long-term goal of understanding the signals that drive premalignant lesions to malignancy. This could provide insight into the development of early-detection and early-interception technologies and involves studying the role of Musashi (Msi), an RNA-binding protein and a cell fate determinant. Msi is highly concentrated in stem cells and is extinguished with differentiation. Msi has been found to increase in the progression of multiple cancer types and therefore might serve as a paradigm for controlling aggressive cancers.

Dr. Reya is collaborating with Dr. Andrew Lowy at the University of California, San Diego, School of Medicine, to examine pancreatic cancer in this context. Pancreatic cancer is the third-leading cause of cancer-related deaths, and the most common treatments are radiation and chemotherapy. A small portion of patients are eligible for surgical treatment. In those patients, however, the cancer tends to return with a survival rate of 11 percent over 5 years. In early stages of pancreatic cancer, cells are differentiated but hyperplastic; at later stages, the cells become undifferentiated. Using a mouse model, the group found that loss of Msi leads to a significant reduction of pancreatic cancer burden. Tumors were reduced in knockout mice, and the lesions were benign. These finding suggest that stem cell pathways could be critically important for driving benign lesions into malignancy.

The Reya laboratory is working with Ionis Pharmaceuticals to develop antisense oligonucleotides to target this pathway for treatment of pancreatic cancers, as well as other cancers, with a strong interest in the function of affected cells. Using crosses between mouse models, they studied heterogeneity within tumors. Treatment with gemcitabine in the mice leads to depletion of reporter-negative cells and increases

in reporter-positive cells. These results could be applied for the development of a new platform to target the drug-resistant cell population.

Over the past several years, Dr. Reya has worked to develop technologies for noninvasive *in vivo* imaging of the tumor microenvironment. Thus far, she has used the platform to examine leukemia and pancreatic cancer. The technologies can be used to study leukemia cells at high resolution and within blood vessels. The leukemia cells appear to develop long-term associations with the tumor microenvironment and derive supportive signals. The Reya laboratory also has reported cellular clusters within pancreatic tumors, suggesting a unique microenvironment within the population.

The Reya laboratory now is working to understand the molecular infrastructure of these drug-resistant cell populations. They are comparing the transcriptomic and epigenetic profiles of reporter-positive and reporter-negative cells, as well as the functional consequences of these pathways. They are performing a genome-wide CRISPR screen within a 3D organoid. They integrated the CRISPR data and RNA-sequencing data to identify genes that are essential for the growth of these populations. They then developed an integrated illustration of multiple pathways that affect drug-resistant populations in pancreatic cancer, including cytokine/immune, RAR-related orphan receptor γ (RORγ). Dr. Reya explained that RORγ inhibition blocks primary pancreatic cancer growth in patients, and pharmacologic blockage of RORγ disrupts stem cell clusters *in vivo*. She emphasized that many components typically associated with the immune system and the tumor microenvironment now are being identified as intrinsic dependencies of pancreatic cancer epithelial cells, particularly in the drug-resistant population. Dr. Reya proposed that some cancers have co-opted the cytokine-rich immunomodulatory milieu, possible reflecting a selective advantage. These immunomodulatory agents could be repositioned for therapeutic applications. She emphasized that the pathways are pleiotropic and should be considered as such.

In the discussion, the following points were made:

- RORγ can trigger interleukin-17, and Dr. Reya's group is using this system to assess the effects of RORγ inhibitors. They have not, however, examined the effects of the RAS, an oncogene mutated in 30 percent of cancers, on this set of pathways and signals. Dr. Reya has observed that Msi increases with RAS activation and p53 deletion.

- Primary tumors are 10 percent reporter positive, and circulating tumor cells are 50 percent reporter positive. These findings suggest that the Msi-expressing cells survive better in hostile environments and therefore might be able to populate other sites. Dr. Reya noted that she was unsure of the mechanism by which the cells exit the tumor.

- Dr. Reya's findings suggest both dispersion of cells and loss in their survival; the dispersion might trigger cell death. Work using RORγ knockout mice suggests a clear intrinsic dependence of the epithelial cell, rather than through the microenvironment.

- Reporter-positive cells can become reporter negative, but reporter-negative cells typically do not become reporter positive in any normal context. The pancreatic intraepithelial neoplasia lesions did not progress to adenocarcinoma in the presence of Msi, suggesting that the lesions are more benign.

- Reporter-positive cells are enriched in mucins, extracellular matrix proteins, and adhesion molecules. These factors might help account for differences in tumor microenvironments around reporter-positive cells. The specific function of the microenvironment around reporter-positive and reporter-negative cells requires further investigation.

VII. RFA/COOP. AGR./RFP and PAR CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

Division of Cancer Control and Population Sciences

Research to Understand and Address the Survivorship Needs of Individuals Living with Advanced Cancer (New RFA)—Dr. Michelle Mollica

Dr. Michelle Mollica, Senior Advisor, Office of Cancer Survivorship, DCCPS, NCI, presented a new RFA concept to better understand and address the survivorship needs of individuals living with likely incurable cancers, focusing on people with advanced or metastatic cancer or those who progress to metastatic cancer. Currently, more than 16 million individuals in the United States have a history of cancer, a number that is expected to grow to more than 26 million by 2040. The group of survivors encompasses many cancer types, and individuals may cycle on or off treatment and have periods with and without active disease. Those with advanced or metastatic cancer receiving targeted therapies or immunotherapies are included in this group. Historically, survivorship initiatives have focused on the period after treatment ends. Most often, individuals living with likely incurable cancer have complex survivorship needs, and associated care is essential from the time of diagnosis forward.

The NCI held a public meeting in May 2021 and conducted an NIH portfolio analysis to identify evidence gaps related to this type of care, including a need to understand the clinical, genomic, and lifestyle factors associated with improved outcomes and better quality of life; the types and trajectories of physical and psychological symptoms; the impact of prognostic awareness on patients and caregivers and strategies to enhance provider communication of prognostic information; the need to develop and test innovative models of health care delivery; and the need for interventional research to determine the best ways to improve quality of life and quality of care for this population.

This RFA will address identified evidence gaps and will include both observational and interventional research. Studies submitted can include any population of individuals living with likely incurable cancer and diagnosed at any age. Populations may be defined by a single diagnosis or multiple primary diagnoses or by cancer treatment modalities or other characteristics as appropriate. Proposed studies must focus on the survivor and measure outcomes at the survivor level, but they also can include caregivers, providers, and health system–level targets. In addition, studies must include appropriate clinical data—including biomarker and radiologic data—to characterize treatment response, toxicities, and disease status. The DCCPS has a strong interest in proposals that include diverse populations and those that focus on individuals who are treated with newer therapies. Currently, the NIH does not have a robust portfolio focused on survivorship of this population. Previous funding opportunity announcements have focused exclusively on end-of-life care, and this RFA will incentivize simultaneous work that will develop a foundation to effectively understand and improve outcomes for this increasing population.

Dr. Mollica summarized that this RFA, a direct response to key gap areas identified by NCI and external stakeholders, has the potential to enhance the understanding of symptoms, care patterns, and unmet needs; increase effective strategies to improve survivorship care delivery; and improve outcomes for the growing number of individuals living with likely incurable cancers.

Subcommittee Review. Dr. Dorothy K. Hatsukami, Associate Director of Cancer Prevention and Control, Masonic Cancer Center, Professor, Department of Psychiatry, University of Minnesota, expressed the Subcommittee's strong support for the concept, which addresses a major gap in the scientific literature and will optimize care among patients living with likely incurable cancer, particularly given the likely increase in this population in the coming years. The Subcommittee appreciated the systematic methods used to identify gaps, the framing of survivorship using the chronic disease paradigm,

the focus on underserved populations, and the recommendation to engage cancer survivors in the grant application.

In the discussion, the following points were made:

- Infrastructure must be developed to support and increase data resources focused on this population to enable researchers to better understand patterns and experiences of care. The RFA is intentionally broad to include both observational and interventional research that will address this gap.

- Although a continuum of people within this population likely will experience different treatment periods and periods with and without disease, the DCCPS acknowledges the heterogenous nature of the population and requests proposals to both understand and address the needs of this broad population.

- Access to treatment varies across groups and determines whether an individual survives with likely incurable cancer; an intentional focus on intersectionality and an exploration of where inequities exist along the journey through survivorship would ensure that the study population is representative of the survivorship experience.

- Although survivors are the main focus of the study, research on caregivers as part of the survivor–caregiver dyad is within scope and would reflect the crucial role of social support in survivorship.

The first-year cost is estimated at $3 M in Year 1 for three R01 awards and $3.5 M in Year 2 for four R01 awards, with a total cost of $32.5 M for 5 years.

Motion. A motion to approve the DCCPS' new RFA entitled "Research to Understand and Address the Survivorship Needs of Individuals Living with Advanced Cancer" was approved unanimously.

Pragmatic Trials Across the Cancer Control Continuum (New PAR)—
Dr. Winnie E. Norton

Dr. Winnie E. Norton, Program Director, DCCPS, NCI, presented a new PAR concept on pragmatic trials across the cancer control continuum. This concept was developed jointly by the DCCPS Pragmatic Trials Team. The purpose is threefold: Expand the portfolio of evidence-based interventions in cancer control and population health; support the design and conduct of pragmatic trials through which such interventions can be tested; and generate information that reflects real-world settings and directly informs practice.

Over the past several decades, the field has made tremendous advances to improve cancer-related outcomes using evidence-based cancer control interventions. These interventions have addressed significant cancer-related issues, such as smoking, diet, physical activity, sun safety, and colorectal screening. Many of these interventions are available for implementation, including the NCI-supported evidence-based cancer control programs that contain more than 200 evidence-based interventions. Although this progress has been significant, several notable gaps in the DCCPS intervention portfolio remain. These include the need for interventions to address populations that are underserved, people from racial and ethnic minority groups, and underresourced communities. A need exists for interventions that focus on economic hardship, cancer-related health misinformation, survivorship care models for people living in rural or remote communities, alcohol misuse among cancer survivors, and shared decision-making for cancer-related screening and treatment.

Tools have been developed to help clinical trialists understand the design elements of an explanatory trial (ideal conditions) or pragmatic trial (usual conditions) to match the purpose and intent of the study. One such tool is the PRagmatic Explanatory Continuum Indicator Summary (PRECIS)—now the validated version PRECIS-2—which consists of nine domains, including eligibility and recruitment, that are scored from 1 (very explanatory) to 5 (very pragmatic). To date, PRECIS-2 has been used in more than 700 registered trials worldwide and has been adapted to practitioner and care delivery–setting trials.

Dr. Norton contrasted a PRECIS-2-designed explanatory and pragmatic trial, emphasizing that a pragmatic study would have eligibility of broad inclusion criteria, be conducted across multiple clinics, and use all available resources, with an intent-to-treat primary analysis. An NCI portfolio analysis of pragmatic trials revealed 29 funded grants over the past 10 fiscal years; 22 were within DCCPS. Most of the studies used a pragmatic trial without any additional context, only seven included any reference to recent advances of how a pragmatic trial can be operationalized, and none included comprehensive descriptions of pragmatic trial design elements.

This proposed concept will support the use of pragmatic trials for testing cancer control interventions using the UG3/UH3 funding mechanism. This research will fill gaps in the DCCPS portfolio of evidence-based interventions in cancer control, especially for populations that are underserved and in communities that are underresourced. Studies will leverage full conceptualization and operationalization of trial design elements (e.g., PRECIS-2) to be more pragmatic than explanatory.

Subcommittee Review. Dr. Karen M. Basen-Engquist, Professor, Department of Behavioral Science, Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, expressed the Subcommittee's support for the concept. The Subcommittee appreciated NCI staff responses to their suggestions to refine the concept to emphasize interventions to address health inequities and health disparities and to underscore essential involvement of collaborators (e.g., community members, public health partners, health care systems, and organizations).

In the discussion, the following points were made:

- This concept focuses on cancer control interventions, but takes into account other research groups and funders (e.g., Patient-Centered Outcomes Research Institute) doing similar work in other contexts.

- Because the infrastructure of the NCI Community Oncology Research Program (NCORP) is designed to sponsor pragmatic trials, this program would be complementary to this PAR.

- The concept should include provisions for supporting the staffing needed (e.g., allied health professionals) to implement interventions for pragmatic trials, extending beyond the existing personnel located at a specific clinical site, particularly for non-treatment trials.

- The funding awarded to CCSG is moving toward a metric of reporting accruals of pragmatic trials, and such trials should be defined clearly for NCI investigators. Hosting an educational session with Cancer Centers directors would be one place to begin.

Motion. A motion to approve the DCCPS' new PAR entitled "Pragmatic Trials across the Cancer Control Continuum" was approved unanimously.

Office of the Director

Outstanding Investigator Award (R35) (New RFA)—Dr. Dinah S. Singer

Dr. Singer presented a new RFA concept, converting the Outstanding Investigator Award (OIA) (R35) from a PAR to an RFA. The goal of the OIA is to encourage accomplished investigators to pursue innovative research directions and to reduce the administrative burden by providing them with long-term support. From 1983 to 1993, the NCI sponsored the Outstanding Investigator Grant (OIG), which had the same goal as the OIA. The OIG had no fixed budget, incorporated all of the grant funding for the principal investigator (PI), and provided 7 years of support. During the lifetime of the OIG, many notable scientists were supported, but the award was discontinued for several reasons. The OIG consolidated all the awardees' funding into one large grant, regardless of the NIH Institute or Center (IC). Because many of the OIG PIs had substantial support from other ICs, which NCI then supported, the cost per award was sizeable. No limit was set on the number of OIGs a PI could have, resulting in funding that grew to more than 11 percent of the RPG pool. Despite these budgetary challenges, the OIG successfully achieved its goal of encouraging accomplished investigators to pursue novel cancer research areas.

Launched in 2015 as a PAR, the OIA was designed to avoid the problems of the OIG. This award provides long-term support for accomplished scientists who have made seminal contributions to cancer research. The OIA enables innovative studies in emerging research areas or that extend previous discoveries in new directions in biomedical, behavioral, or clinical cancer research. The OIA requires that eligible PIs be highly accomplished and have had an NCI grant award for the last 5 consecutive fiscal years. Only NCI grants are required to be relinquished when the OIA is awarded. In addition, the institution must demonstrate a commitment to the PI, such as by providing 20 percent salary support for the award duration.

The review criteria for the OIA differs markedly from the standard R01. Instead of specific aims, the focus is on the investigator's scientific accomplishments and overall vision for future directions. Specifically, successful OIA applicants should have (1) articulated a compelling vision of the future direction of their research; (2) track records of outstanding cancer research accomplishments and productivity; (3) seminal contributions that led to groundbreaking or paradigm-shifting concepts in cancer research; and (4) the potential to continue to be leaders in cancer research with significant impact and influence on cancer research. In terms of requirements, PIs must commit at least 50 percent of their time to the OIA, are limited to two additional NCI-funded grants, and are expected to serve as peer reviewers if invited. Since 2015, the NCI has funded 176 OIA grants, with an average of 17 awards made annually from FY 2018 to FY 2021.

Dr. Singer reviewed lessons learned from FY 2015 to FY 2021 OIA awards. Regarding post-award productivity, the publication rates from the first cohort (the only one funded to allow these analyses) to subsequent cohorts, before and after the award, was maintained. Using citation rate as a surrogate for impact, 75 percent of all R35 awards had at least one publication in the top 1 percent of cited publications and nearly 97 percent had at least one publication in the top 10 percent, which is significantly higher than all other R01 comparison groups evaluated.

In terms of demographics, the gender breakdown of awardees reflects the applicant pool, with only 19 percent identifying as female, which is in contrast to the eligible pool, of whom 29 percent are female. Data showed that eligible women are not applying. The numbers of underrepresented minorities are too small to present. Among eligible PIs, within 10 years of their first award, less than 5 percent apply, suggesting that the OIA is viewed as an advanced career award rather than one that also includes mid-career investigators. Across the perspective of scientific areas supported by the OIA as defined by assignment to Divisions, more than 90 percent of the applications come from either the Division of Cancer Biology or the Division of Cancer Treatment and Diagnosis (DCTD). DCP and DCCPS applicants

are underrepresented, even when corrected for the differences in the sizes of the portfolios in the different Divisions. When applicants from DCP or DCCPS do apply, their success rates are comparable to those of applicants from the other two Divisions.

Evaluating programmatic expenditures, which are the incremental costs of the OIA, required calculating average costs across funding mechanisms. The average total cost of an NCI R01 is $520,000; the average total cost of an OIA is $935,000. The incremental cost of the OIA per PI is approximately $400,000. For a total of 17 awards, the average incremental cost of the OIA program is about $7 million per year. Dr. Singer emphasized that this probably represents an overestimate to the actual cost because the calculation does not take into account institutions that have to relinquish existing NCI awards when the OIA is awarded. The majority of OIAs have no additional R01 equivalent beyond their OIA. Only 10 percent had one more R01, which is comparable to PIs whose R01s scored in the 1–3 percentile rank. Dr. Singer summarized that the OIA program is successful scientifically. The NCI needs to be more proactive in recruiting mid-career investigators, women, and underrepresented minorities, as well as prevention and population scientists. In terms of programmatic cost, the incremental cost of the entire program is estimated at $7 M, with most of the funded PIs having had only NCI awards.

The current OIA was intended to be a pilot, and the PAR has been effective in allowing the NCI to test the program. Unlike an RFA, in a PAR, the selection of awardees is entirely score driven, with no flexibility in balancing the portfolio between new and competing awards, no flexibility in balancing demographics, and no flexibility in maintaining a steady-state level of awards. This proposed RFA concept will replace the PAR. The fundamental structure of the award will not change. The OIA program will be evaluated at the end of the funding period. The criteria will include an assessment of the importance of the contributions made by the OIA program and the success in improving the demographics.

Subcommittee Review. Dr. Shelton Earp, Director, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, Director, UNC Cancer Care, The University of North Carolina at Chapel Hill, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Earp highlighted that the OIA accomplishments are clear and that the OIA is a sound investment for the NCI, given the return of quality grants. Questions remain about whether a 7-year grant for younger PIs would resolve some of the existing problems. The Subcommittee appreciated the update on the plans for the program and the detailed analysis of grant demographics and suggested expanding funding.

In the discussion, the following points were made:

- The rationale to not include provisions for clinical trials was based on the OIA individual budgets, but these can be considered in the future.

- The opportunity exists for population scientists to participate, but the study section reviewers are concentrated heavily in the basic and clinical science disciplines. The key is to engage this community to apply, which will change the representation and composition of the study section.

- The requirement for 5 years of consecutive funding is restrictive regarding renewals, but investigators are allowed to have two additional R01 grants to compensate for a missed cycle of support.

- The gender imbalance in applications is NIH-wide, with little change over the past 10 years. The NCI could take an innovative approach to capitalize on the institutional nomination process to encourage OIA applications from the underrepresented groups.

The first year's cost is estimated at $17 M for 17 to 18 R35 awards, with a total cost of $119 M for 7 years.

Motion. A motion to approve the Office of the Director's (OD) new RFA entitled "Outstanding Investigator Award (R35)" was approved unanimously.

VIII. ADJOURNMENT—DR. KEITH T. FLAHERTY

Dr. Flaherty adjourned Day 1 of the 6th BSA meeting.

TUESDAY, 29 MARCH 2022

IX. CALL TO ORDER AND OPENING REMARKS—DR. KEITH T. FLAHERTY

Dr. Flaherty called to order Day 2 of the 6th BSA meeting and welcomed members of the Board, NCI staff, and guests.

X. RFA/COOP. AGR./RFP and PAR CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

Division of Cancer Treatment and Diagnosis

Precision Approaches in Radiation Synthetic combinations (PAIRS) (New PAR)— Dr. Michael G. Espey

Dr. Michael G. Espey, Chief, Radiotherapy Development Branch, Radiation Research Program, DCTD, NCI, presented a new PAR concept on PAIRS to support research focused on targeting vulnerabilities created by cancer reprogramming associated with responses to radiation–drug combination therapy. PAIRS seeks to catalyze information in interdisciplinary teams, with the goal of strengthening the translation of meritorious research that uniquely brings radiation into targeted synthetic combination strategies. For more than 20 years, researchers have used synthetic lethality approaches in cancer drug discovery and have evaluated such a strategy against undruggable or loss-of-function mutations. The synthetic lethality scenario occurs when a mutation in one of two interacting genes is viable, but mutation of both results in lethality. Dr. Espey emphasized that the mapping of essentiality relationships is well suited to today's genetic and drug screening approaches in a systems biology framework. PAIRS builds on the conception of synthetic lethality, relating cancer reprogramming to conditional radiation treatment synthetic combinations. Reprogramming adds robustness and buffers cancer cells against underlying genetic mutations. Ionizing radiation is a standard-of-care component for greater than 50 percent of all cancers, and emerging opportunities exist in the radiopharmaceutical arena. Radiation treatment can precisely trigger essentiality demands on cancer-selective networks.

The core of this PAR concept is that radiation can be leveraged as a precision tool in conditional synthetic combination designs. The scope of this research extends from preclinical to early clinical trials research and seeks to exploit opportunities in synthetic combination treatment strategies that pair radiation treatment with targeted agents. Radiation treatment/conditional synthetic combinations have been used to exploit intrinsic vulnerability in patients with glioma cancer harboring the isocitrate dehydrogenase mutation, as well as adaptive vulnerability in preclinical xenograft studies of prostate cancer. Strong links between essentiality and radiation treatment response suggest that timely opportunities exist that are not being explored adequately in the preclinical to early translational areas.

A portfolio analysis of synthetic lethality or synthetic combination research at NCI revealed 38 active synthetic lethality R01 awards in the Developmental Therapeutics Program, but few projects involved a radiation treatment–synthetic combination. This PAR seeks projects that pair radiation with diverse, druggable, synthetic combination targets. PAIRS proposes to populate the NCI portfolio with meritorious projects that advance development and translation of strategies leveraging the unique precision qualities of radiation therapy in creating synthetic combination vulnerabilities using the R01 (clinical trials allowed) and R21 funding mechanisms.

Subcommittee Review. Dr. Karen M. Mustian, Dean's Distinguished Endowed Professor of Oncology and Surgery, Departments of Surgery, Radiation Oncology, and Public Health Sciences, University of Rochester School of Medicine and Dentistry, expressed the Subcommittee's strong support for the PAR concept, which addresses a major gap. The Subcommittee appreciated NCI staff for responding to their suggestions to refine the synthetic lethality terminology, clearly define the scope, and identify success metrics.

In the discussion, the following points were made:

- The objective is to build upon existing NCI programs and initiatives in this area, such as the Centers for Cancer Systems Biology (CCSB) and the Radiation Oncology-Biology Integration Network (ROBIN).

- The PAR is not taking a top-down approach but is agnostic to the type of radiation (e.g., radionuclide or external beam) an applicant proposes, because that source is integral to the strategy for the combination.

Motion. A motion to approve the DCTD's new PAR entitled "Precision Approaches in Radiation Synthetic Combinations (PAIRS)" was approved unanimously.

Cancer Adoptive Cellular Therapy Network (Can-ACT) (New RFA/Coop. Agr)—
Dr. Marc Ernstoff

Dr. Marc Ernstoff, Medical Officer, Chief of the ImmunoOncology Branch, DCTD, NCI, presented a new RFA to establish the Can-ACT network. Cell therapies were identified as a priority topic by the NCAB *ad hoc* Subcommittee on Experimental Therapeutics, which led to workshops on Cell-Based Immunotherapy for Solid Tumors in 2018 and 2020. During the 2020 workshop, participants identified seven areas of unmet need, including preclinical and translational research to advance cell therapy for solid tumors in both adult and pediatric patients; small proof-of-concept studies to gain quick knowledge of promising new treatment approaches; enhancement of cell manufacturing technologies; and identification of biomarkers and imaging-based detection of response to therapy. Needed services identified were standardization of the cell product characterization through a core laboratory, quality-control testing of cell therapy–related reagents needed for manufacturing, and guidance for investigators to prepare investigational new drug submissions to the FDA.

To address unmet needs in cell therapies, the NCI established cell therapy–related manufacturing resources at the Frederick National Laboratory for Cancer Research (FNLCR). The current facility at the FNLCR contains two Good Manufacturing Practice (GMP) suites, with a new facility under construction to house an additional three GMP suites due to be completed by the fall or winter of 2022. Currently available technologies include genetically modified autologous cells, as well as lentivirus and gamma retrovirus vectors; G-Rex® manufacturing platforms and CRISPR-based gene-editing technologies are expected to be available in 2023. The current capacity of these cell therapy resources enables the completion of four cell therapy products per month and four viral vector campaigns per year; the future added capacity is expected to increase outputs to 12 cell therapy products per month and eight virus

vector campaigns per year. In addition, a cell therapy core service is in development. This core will provide quality systems and regulatory affairs guidance, multisite trial GMP production support, clinical trials coordination, and data coordination.

A portfolio analysis of solid tumor adopted cell therapy trials based on data from the Coordinating Center for Clinical Trials, Office of the Director, NCI, showed a paucity of NCI-funded therapies. The majority of the trials investigated hematopoietic and lymphoid neoplasms. Thirty-six of the Cancer Centers have ongoing cell therapy programs. The purpose of this RFA is to foster innovation and promote early-stage clinical testing of novel state-of-the-art cell-based immunotherapies for solid tumors in adults and pediatric patients and leverage the NCI resources to support the cell therapy community. The Can-ACT goals are fivefold: (1) Develop and enhance immune cellular products modified genetically or through other manipulations for the treatment of adult and pediatric patients with solid tumors; (2) support early-phase clinical trials; (3) explore imaging and biomarker development; (4) expand understanding of the mechanism of action, as well as natural and acquired resistance; and (5) evaluate strategies to modulate the immunosuppressive tumor microenvironment. This RFA will support a U24 coordinating center, two adult and two pediatric UG3/UH3 centers, and the FNLCR Immune Cell Network (ICN) Core starting in the third year of funding.

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 RFA concept. The Subcommittee appreciates NCI staff responses to their concerns of ensuring that the RFA attracts the intended applicant pool and is focusing on preclinical modeling, with the opportunity for conducting an early-phase clinical trial.

In the discussion, the following points were made:

- Although this proposed RFA is not responsive to investigations of bispecific T-cell engagers, the NCI acknowledges the advances in this area of research and the emerging therapies.

- Cancer Centers and/or networks that have limited-to-no cellular therapy capabilities could potentially apply jointly.

The first year's cost is estimated at $5 M for three UG3/UH3 awards and one U24 award in Year 1, $12 M for four UG3UH3 awards in Year 2, and $ 20 M in Years 3–6 for four UG3UH3 awards and the FNLCR ICN, with a total cost of $96 M for 6 years.

Motion: A motion to approve the DCTD's new RFA/Coop. Agr. entitled "Cancer Adoptive Cellular Therapy Network (Can-ACT)" was approved unanimously.

Cancer Immune Monitoring and Analysis Centers and Cancer Immunologic Data Commons (CIMAC-CIDC) Network (Re-Issue RFA/Coop. Agr./Limited Competition)—Dr. Magdalena Thurin and Mr. David Patton

BSA Chair Dr. Flaherty recused himself due to a conflict of interest. Dr. Leslie L. Robison, Chairman, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center, presided as Chair for the consideration of this concept.

Dr. Magdalena Thurin, Program Director, DCTD, NCI, presented a re-issue RFA concept for the CIMAC-CIDC Network. A critical need exists to identify actionable biomarkers to improve the efficacy and safety of immunotherapy approaches to better identify which patients will benefit from the therapy. Multiple scientific and technical challenges limit biomarker research, including the need for innovative

multimodal analysis to address the complexities of tumor–immune system interface and treatment modalities. Interlaboratory assay performance and data variability exists. Furthermore, clinical outcome data, centralized bioinformatic pipelines, and databases are needed to conduct cross-trial and integrative analysis to develop predictive models.

To address this critical need and accompanying challenges, the NCI, in 2017, established the CIMAC-CIDC Network. In 2018, the Network was joined by the Partnership for Accelerating Cancer Therapies (PACT), a 5-year public–private partnership between the NCI and 12 pharmaceutical companies interested in promoting immuno-oncology. During the current funding period, PACT provided support to multiple functions of the network. The scientific goals of CIMAC-CIDC are to provide an understanding of the mechanism of action of immunotherapy agents and to identify determinants driving response, resistance, and toxicity in the NCI immunotherapy trials. The objectives are to establish an operational infrastructure, provide validated and harmonized multimodality assays, develop pipelines for data analysis, establish a database of clinically annotated biomarkers, and facilitate data sharing. The Network consists of four academic laboratory centers (CIMACs), a data coordination center, clinical trials groups, and CIMAC laboratories.

Dr. Thurin highlighted the accomplishments of the program. Regarding assays and standards, the Network harmonized Tier 1 assays to ensure comparability and data reporting across trials; validated all assays, standard operating procedures, and harmonization guidelines made available to the scientific community; developed a specimen collection umbrella protocol to minimize preanalytical variability and enhance accuracy of biomarker assays; and developed standards to monitor longitudinal assay performance. In an iterative process, the Network completed Tier 1 assay harmonization across the CIMACs to reduce variability in data sets generated across different laboratories. The Network collaborated on 35 immuno-oncology trials, enrolling more than 2,000 patients across the NCI clinical trial networks, including the NCI's National Clinical Trials Network (NCTN).

Mr. David Patton, Associate Director of Clinical Research Programs, Informatics and Data Science Program, Center for Biomedical Informatics and Information Technology (CBIIT), NCI, explained that the CIDC was established with a bioinformatics and cloud-based information technology infrastructure for the Network. The CIDC maintains the data and data warehousing with security and access control and deposits data into the NCI data-sharing repositories. In the next phase, the CIDC will expand bioinformatics pipelines and support future cross-trial analyses and data sharing. The Correlative Sample Management System (CSMS) provides specimen management across the Network, has managed more than 7,000 samples, and is funded by the PACT for the key functionalities.

This re-issue RFA continues the CIMAC-CIDC and will support system maintenance (security, operations, and maintenance), training and coordination, system upgrades and a help desk, and modules for new assays for the CSMS. A formalized Operations Center for Central Coordination is proposed to fill the need for central coordination across the Network for correlative studies and administrative tasks.

Subcommittee Review. Dr. Robert H. Vonderheide, Director, Abramson Cancer Center, Vice Dean, Cancer Programs, Perelman School of Medicine, Vice President, Cancer Programs, University of Pennsylvania Health System, John H. Glick, MD Abramson Cancer Center, Director's Professor Perelman School of Medicine, University of Pennsylvania, expressed the Subcommittee's support for the re-issue concept. Dr. Vonderheide noted that the concept remains important for the NCI and its vision for immuno-oncology precision medicine. The Subcommittee agrees with the program's expanding its enabling capabilities to include additional bioinformatics and central coordination for correlative studies.

In the discussion, the following point was made:

- Multiple samples from an individual patient, when deposited, are linked within the NCI data-sharing repositories (e.g., Cancer Research Data Commons).

The first-year cost for the one-time issuance is estimated at $12.35 M for five U24 awards, with a total cost of $61.75 M for 5 years.

Motion. A motion to concur on the re-issuance of the DCTD's RFA/Coop. Agr. entitled "Cancer Immune Monitoring and Analysis Centers and Cancer Immunologic Data Commons (CIMAC-CIDC) Network" was approved with 23 ayes, zero nays, and 3 abstentions.

Office of the Director

Small Business Innovation Research (SBIR) Contract Topics (New RFP)— Ms. Deepa Narayanan

Ms. Deepa Narayanan, Program Director and Team Leader, SBIR Development Center, presented nine SBIR research and development (R&D) contract topics for funding in FY 2023. The NCI SBIR budget is a congressionally set-aside allotment of 3.65 percent of the overall NCI appropriations. The SBIR program supports promising startup companies with SBIR and STTR grants that are investigator initiated and SBIR contracts. The NCI topics are developed once each calendar year to include in the NIH-wide SBIR contract RFPs. Typically, the NCI contributes 10 to 20 new topics, representing 10–25 percent of the NCI SBIR/STTR budget. In FY 2021, the NCI allocated $21 M (12 percent) of the $161 M budget to R&D contracts. Ms. Narayanan explained that contract solicitation is one way to programmatically balance the NCI portfolio and support key NCI priority areas. Program officers across the NCI help identify specific needs in the cancer community that can be addressed using R&D contracts. In addition, R&D contracts are used to stimulate commercialization in emerging areas; streamline stepwise product development; and support technology transfer from NIH laboratories to industry. The contract topics are diverse and serve needs beyond just the NCI. All products that are developed must fulfill a commercial necessity.

Identifying the contract topics is an NCI-wide process. Each October, the SBIR Development Center solicits ideas for new contract proposals from across the NCI. Topics are submitted from program directors from the NCI Divisions, Offices, and Centers and also from the FDA Center for Devices and Radiological Health. Submitted topics then are evaluated by two NCI technology advisory group (TAG) panels composed of subject-matter experts from across the NCI. The TAG panels evaluate the submitted topics for innovation and concept, commercialization potential, and the ability to have a significant benefit for cancer patients, providers, or caregivers. The reviewers ensure that no duplication exists in the NCI SBIR portfolio and that re-issued topics are justified appropriately. In FY 2022, a new feature was added to include a market analysis for each topic performed by business students before the TAG review, and that report was submitted to the internal reviewers. The nine topics selected reflect NCI priority areas, commercial potential, and portfolio gaps. These fall into the areas of therapeutics, medical devices, diagnostics, and information technology. BSA members were reminded that Phase I awards provide up to $300,000 for 6 months (SBIR) to 1 year (STTR), and Phase II awards provide up to $2 million over 2 years. Ms. Narayanan summarized the nine topics and overall goals, noting that detailed reports have been provided in the electronic Board book.

Therapeutics Topics

Development of Senotherapeutic Agents for Cancer Treatment. Support the basic and preclinical development of senotherapeutic agents for research, neoadjuvant, adjuvant, or combination cancer therapy; this is a re-issue topic.

Medical Devices Topics

Non-Invasive Device Technology Research and Development for Chemotherapy-Induced Peripheral Neuropathy (CIPN) Management. Advance the development of innovative non-invasive device technologies to provide effective mitigation of CIPN in a non-invasive, cost-effective, accessible manner in the home-care setting.

Wearable Devices for Dosimetry of Radiopharmaceutical Therapy. Develop wearable technologies (e.g., dosimetry sensor–incorporated clothing) to allow the radiopharmaceutical therapy (RPT) dose to be continuously measured, providing rich, time-based dose data for RPT agents that can be correlated with the patient's anatomy.

Wearable Technologies to Facilitate Remote Monitoring of Cancer Patients Following Treatment. Improve the availability of new or better remote monitoring tools for patients and their clinical care teams during sensitive periods of treatment, with a view to improved health-related quality of life and reduced costs associated with further hospital visits.

Clinical Diagnostics and Molecular Analysis Topics

Technology Platforms for Circulating Tumor-Macrophage Hybrid Cells (cTMHCs). Support the development of platforms to isolate, enrich, enumerate, and identify the cTMHCs in blood from cancer patients or animal models of cancer. This contract topic aims to enable a thorough understanding of the biology of cTHMCs in metastasis and provide a novel means to remotely monitor cancer progression and metastasis.

Rapid and Affordable Point-of-Care HPV Diagnostics for Cervical Cancer Control. Advance the development of new alternatives for HPV testing to the market that are both in a form and at a price point that will enable self-testing programs to be established globally.

Translation of Novel Cancer-Specific Imaging Agents and Techniques to Mediate Successful Image-Guided Cancer Interventions. Support the translation of novel activatable agents and techniques for sensitive cancer detection in human subjects.

Information Technology and Bioinformatics Topics

Digital Tools to Integrate Cancer Prevention Within Primary Care. Develop a digital platform that provides primary care physicians with validated cancer risk assessment tools, cancer prevention guidelines, and clinical recommendations based on a patient's risk factors to discuss with their patients.

Software to Evaluate Artificial Intelligence (AI)/Machine Learning (ML) Medical Devices in Oncology Settings. Stimulate the participation of small businesses in the FDA's Medical Device Development Tool program to develop software tools for evaluating and monitoring AI/ML devices in oncology settings.

SBIR R&D Contracts: Impact and Success Stories

Ms. Narayanan highlighted a few commercial products resulting from previous and existing SBIR R&D contracts. DiaCarta developed RadTox™, which is a diagnostic test to monitor radiation toxicity in cancer

patients currently being sold outside the United States. CivaTech Oncology, Inc., was awarded SBIR Phase I and Phase II grants to develop and validate CivaSheet®, a customizable, implantable, unidirectional brachytherapy device/sheet. This device is FDA, NRC, and 510(K) approved, commercially available, and being used in clinics to treat lung, pancreas, colorectal, sarcoma, and head and neck cancers. Medable, Inc., developed a digital decentralized clinical trial platform for global clinical trials. In November 2020, Medable announced $91 M in new funding from investors to accelerate its platform, signifying industry's interest in digital and decentralized clinical trials.

Subcommittee Review. Dr. David Sidransky, Director, Head and Neck Cancer Research, Professor of Otolaryngology-Head and Neck Surgery, Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, expressed the Subcommittee's strong support for the concept. Dr. Sidransky noted the Subcommittee's enthusiasm for the addition of the FDA input, as well as the market survey, which enhances the breadth and width of the way the topics are selected. The Subcommittee commended the NCI on this innovative and critical program that is demonstrating true translational science and research, from grants to publications to companies' producing products beneficial to cancer patients in the community.

In the discussion, the following points were made:

- Three compelling reasons speak to the need for consideration of SBIRs and STTRs that are promoting the development of low-cost surgical devices. First, 80 percent of solid tumors will require a minimum of one surgical intervention, some more than one. Second, health care in the United States and globally has become expensive. Third, financial toxicity exists and, in many parts of the world, one cancer procedure can result in financial bankruptcy.

- Previous NCI SBIR topics have focused on a more global health perspective on medical devices in general and responses to those solicitations were robust.

Motion. A motion to approve the OD's RFP entitled "SBIR Contract Topics" was approved unanimously.

XI. ON GOING AND NEW BUSINESS— DR. KEITH T. FLAHERTY

The BSA members suggested future presentations on the impact of long COVID-19 on cancer initiation and development and the NIH "Long COVID" initiative; clinical trial capabilities and national response to factors (e.g., personnel attrition) impeding research progress; NCI clinical trial recruitment and representation, including supportive care trials; cancer burden in low- and middle-income countries and the dedicated funding to support this area of research; equity and inclusion language relative to the NCI's funding initiatives; environmental and climate change effects on cancer care; and the Human Tumor Atlas Network and DCP follow-on program. Members were asked to forward any additional suggestions for potential future agenda items to Drs. Flaherty and Gray.

XII. ADJOURNMENT—DR. KEITH T. FLAHERTY

There being no further business, the 6th virtual meeting of the BSA was adjourned at 2:47 p.m. on Tuesday, 29 March 2022.

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Date	Keith T. Flaherty, M.D. Chair, Board of Scientific Advisors
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Date	Paulette S. Gray, Ph.D. Executive Secretary, Board of Scientific Advisors