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

59th Meeting

BOARD OF SCIENTIFIC ADVISORS

Summary of Meeting
25 March 2019

Conference Room TE 406, East Wing
Shady Grove Campus
National Institutes of Health
Bethesda, Maryland

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

BOARD OF SCIENTIFIC ADVISORS

SUMMARY OF MEETING
25 March 2019

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 59th regular meeting on Monday, 25 March 2019, at 9:00 a.m. in Conference Room TE406, East Wing, Shady Grove Campus, National Institutes of Health (NIH), Bethesda, MD. Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President and Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology and Medicine, New York University (NYU) Langone Health, NYU School of Medicine, presided as Chair. The meeting was open to the public from 9:00 a.m. until 4:16 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 reissue concepts presented by NCI Program staff. The agenda also included the NCI Director's, Legislative, and NCI Bio-specimen Tissue Banking reports.

BSA Board Members Present:

Dr. Dafna Bar-Sagi (Chair)
Dr. Michael John Becich
Dr. Mary C. Beckerle
Dr. Melissa Bondy
Dr. Otis W. Brawley*
Dr. Graham A. Colditz
Dr. Carol E. Ferrans
Dr. Keith T. Flaherty*
Dr. Karen E. Knudsen
Dr. James V. Lacey, Jr.
Dr. Michelle M. Le Beau
Dr. Sylvia Katina Plevritis
Dr. Diane Zipursky Quale
Dr. W. Kimryn Rathmell
Dr. Leslie L. Robison*
Dr. Martine F. Roussel
Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon
Dr. David Sidransky*
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson
Dr. Robert H. Vonderheide
Dr. Eileen P. White
Dr. Cheryl L. Willman

Board Members Absent:

Dr. Kenneth C. Anderson
Dr. Christopher M. Counter
Dr. Robert D. Schreiber
Dr. Kevin P. White

* Pending appointment

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

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I. CALL TO ORDER AND OPENING REMARKS—DR. DAFNA BAR-SAGI

Dr. Dafna Bar-Sagi called to order the 59th regular meeting of the BSA and welcomed current members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Bar-Sagi reminded 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. Bar-Sagi noted the approved minutes of the 4 December 2018 Joint BSA/National Cancer Advisory Board (NCAB) meeting and the future meeting dates in the Board book and on the agenda.

Motion. A motion to approve the 2021 meeting dates of the BSA was approved unanimously.

II. NCI DIRECTOR'S REPORT—DRS. NORMAN E. SHARPLESS AND DOUGLAS R. LOWY

Dr. Norman E. Sharpless, Director, NCI, welcomed BSA members and attendees to the 59th meeting of the BSA and provided an update on the NCI progress for the past 18 months, including cancer research accomplishments and achievements in the NCI key focus areas. Dr. Sharpless was joined by Dr. Douglas R. Lowy, Deputy Director, NCI, who provided an update on the NCI budget as well as new and ongoing activities. Dr. Sharpless announced his appointment as Acting Commissioner of the U.S. Food and Drug Administration (FDA) and that he would be transitioning to that office in early April 2019. He noted that Dr. Lowy would become the Acting NCI Director.

Dr. Sharpless acknowledged new BSA members and introduced them: Dr. Mary C. Beckerle, Jon M. Huntsman Presidential Endowed Chair, Distinguished Professor of Biology, Chief Executive Officer, Huntsman Cancer Institute, Associate Vice President of Cancer Affairs, The University of Utah; Dr. Otis W. Brawley, Bloomberg Distinguished Professor of Oncology and Epidemiology, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University; Dr. Keith T. Flaherty, Director, Henri and Belinda Termeer Center for Target Therapy, Director of Clinical Research, Massachusetts General Hospital Cancer Center; Dr. Karen E. Knudsen, Hilary Koprowski Endowed Professor, Chair, Department of Cancer Biology, Director, Sidney Kimmel Cancer Center, Thomas Jefferson University; Dr. Michelle M. Le Beau, Arthur and Marian Edelstein Professor of Medicine, Director, University of Chicago Comprehensive Cancer Center, The University of Chicago; Dr. W. Kimryn Rathmell, Cornelius A. Craig Professor, Department of Medicine, Director, Division of Hematology and Oncology, Vanderbilt University Medical Center; Dr. Leslie L. Robison, Chairman, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center; 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; and, Dr. Robert H. Vonderheide, John H. Glick MD Abramson Cancer Center's Professor, Professor of Medicine, Perelman School of Medicine, Director, Abramson Cancer Center, University of Pennsylvania.

Accomplishments in Advancing Cancer Research. Dr. Sharpless reported that this is a distinctive time for cancer research compared with other areas of biomedical research. The most compelling NCI Surveillance, Epidemiology, and End Results (SEER data show a steady decline in cancer mortality in the United States from the early 1990s to 2015, for patients of all ages, races, and genders. From an industry perspective regarding pharmaceutical innovation, oncology drug development continues to advance despite the long drug-approval cycles and modest success rates of developing new cancer therapeutics. In addition, investments from both the NCI and the pharmaceutical industry have powered a high number of FDA cancer drug approvals in 2018. These advances reflect the increased understanding of cancer biology experienced in the past two decades and enhanced therapeutic approaches have resulted in investigating cancer mutations in a precision medicine approach. For example, in melanoma, despite the 2 percent increased annual incidence from 2000 to 2005, the mortality rates declined by 5 percent per year from 2012 to 2015. Although the outlook is promising and has increased new enthusiasm in cancer research, the unintended consequences are that the increase in NCI grant applications have outpaced the growth of the Research Project Grant (RPG) Pool funding, which supports investigator-initiated research grants (i.e., R01s, P01s, R21s) and established paylines. The NCI is reviewing additional strategies to address RPG Pool funding and reduced paylines, and Dr. Lowy is leading this effort. A full report is planned for the 9-11 June 2019 Joint BSA/NCAB meeting.

Achievements in the NCI Key Focus Areas. Dr. Sharpless remarked that at the beginning of his tenure as NCI Director, the progress in cancer research and commitment to basic science, which resulted in translational science, new therapeutics, and increased understanding in prevention, was well underway at the NCI. To continue this momentum, the NCI identified four key focus areas—basic science, workforce

development, big data, and clinical trials—as opportunities for progress to accelerate cancer research. Workforce development and training of the next generation of cancer researchers remain at the forefront for the NCI. In fiscal year (FY) 2018, the NCI successfully implemented the Method to Extend Research Time (MERIT) award and increased the early-stage investigator (ESI) paylines to the 14th percentile, resulting in a 25 percent increase in ESI R01s. Both of these efforts are continuing in FY 2019.

Dr. Sharpless informed members that new initiatives, RFAs, and investments, including gradual annual increases in funding to the RPG Pool, are an indication of NCI's commitment to basic science. There was a $170 million (M) increase over the FY 2017 enacted level in RPG funding in FY 2018, its largest increase since 2003. Much of the increase supported non-competing continuation (Type 5) awards. The overall increase in the NCI FY 2019 regular appropriations was $179 M, of which $100 M was allotted for the Cancer Moonshot^{SM}. The NCI anticipates adding $100 M to the RPG Pool in FY 2019. Although not sustainable in the long term without further increases in NCI regular appropriations, strategies are being implemented, including making a five percent across-the-board reduction in funding for NCI Divisions, Offices (DOCs), and Centers and ending some programs early. These strategies will uncommit dollars and prioritize in other areas, including the RPG Pool and NCI-designated Cancer Center (Cancer Center) training grants.

Clinical trials are another area in which the NCI has a large portfolio. It has, however, been under-resourced. The intentions in the cancer research community are noble, the science is worthy, but the process has been slow, and funding limited. To address these challenges, the NCI increased funding to the Early Therapeutic Clinical Trials Network (ETCTN) and supporting infrastructures, such as the NCI National Clinical Trials Network (NCTN) Biospecimen Banks (NCTN Banks). The NCI also focused on modernizing trials and making cancer trials more accessible to patients, conducting trials that did not compete with but were complementary to industry-sponsored trials, and enhancing the accrual process, especially for precision trials (e.g., the NCI Molecular Analysis for Therapy Choice [NCI MATCH] trial).

Regarding initiatives on big data, Dr. Sharpless remarked that the NCI is one of the leading federal agencies in the usage of data and the use of cutting-edge approaches for data linkages. Efforts have focused on addressing private and secure data sharing and maximizing use across the extramural cancer research community. Many of the Cancer Moonshot^{SM} initiatives focus on big data, and NCI's data infrastructure investments in the Cancer Genomics Cloud Pilots, SEER contracts, and Genomic Data Commons (GDC) are ongoing. He stated that the Childhood Cancer Data Initiative (Initiative), which was announced at the President's 5 February 2019 State of the Union Address, is one that the NCI anticipates will be appropriated in the FY 2020 budget. The Initiative addresses data infrastructure, interoperability, and acquisition of pediatric cancer patient outcomes data for advancing research. Dr. Sharpless attended a White House meeting hosted by Vice President Michael R. Pence, in which the Vice President conveyed to attendees, childhood cancer survivors, pediatric patients currently undergoing treatment, and their families, the Administration's commitment to advancing childhood cancer research. The Vice President is confident that Congress will support the necessary funding appropriations in the FY 2020 budget.

Dr. Sharpless reflected on his time as NCI Director and the progress made in advancing cancer research. Although grateful for the opportunity to serve the FDA, he will remain interested in the future of many NCI initiatives. Dr. Sharpless stated that he is confident that the NCI will be in capable hands under the leadership of Dr. Lowy, whose past performance as Acting NCI Director from 2015 to 2017 was exemplary.

NCI Appropriations and Budget. Dr. Lowy reminded BSA members that the Cancer Moonshot^{SM} appropriation of $400 M for FY 2019 will be the highest of the $1.8 billion (B), seven-year funding period for the program. Beginning in FY 2020, the annual allotments will decrease by $200 M per year until the funding ends in 2024. The NCI will need to plan carefully for the anticipated decreases, leading up to the final year of Cancer Moonshot^{SM} appropriations. Dr. Lowy reminded members that the NCI

regular appropriations had increased steadily since FY 2015 and that separate appropriations for the Cancer Moonshot℠ were included in the NCI budget in FY 2017. The BSA members were informed that the release of the President's proposed FY 2020 budget on 18 March 2019 marks the first step of the NCI/NIH budget process for the regular appropriations. The FY 2020 proposed budget includes a decrease in the NCI budget compared with the FY 2019 enacted budget. The House and Senate Appropriations Subcommittees on Labor, Health and Human Services, Education, and Related Agencies (L-HHS) budget hearings are scheduled for April 2019. Dr. Lowy stated that he would attend and testify at both hearings.

New and Ongoing Activities. Dr. Lowy noted NCI's ongoing recruitment efforts for directors for the Center for Global Health, Center for Biomedical Informatics and Information Technology, Cancer Therapy Evaluation Program, and Division of Cancer Prevention (DCP). He announced that Dr. Sara Hook, Program Officer for National Missions, Contracting Officer Representative, NCI, has been appointed Associate Director of the Frederick National Laboratory for Cancer Research. Dr. Hook has been at the NCI since 2010 and has shown dedication, commitment, and excellence in her interactions at NCI-Frederick, especially with the RAS Initiative and Cryo-Electron Microscopy Facility.

Members were informed that Drs. Sharpless and Lowy will deliver remarks at the opening ceremony at the 2019 American Association for Cancer Research Annual Meeting being held on March 29-April 3, 2019, in Atlanta, GA. Other NCI staff also will be in attendance to support the NCI/NIH-sponsored sessions, symposia, and plenary sessions.

In the discussion, the following points were made:

- The bipartisan support for cancer research has been strong, but it is up to Congress to decide on additional funding for a second cancer moonshot. Given the lower than desired paylines, exactly how any new commitments to science would impact cancer research and at the same time leverage prior successes would be one argument to make to Congress.

- Approximately 16,000 cases of childhood cancer are reported annually in the United States, the treatment outcomes are heterogeneous, and rare cancers exist. Dr. Sharpless and the NCI think the pediatric cancer population is, therefore, the optimally sized data set and the right area for a data science initiative and data aggregation project. The NCI envisions that this effort will inform the broader data science and cancer research communities.

- Since the Cancer Moonshot investments are underway, it would be a good time for the NCI to assess the transformative influence of the initiative to cancer research. The NCI could consider an update on the progress and impact of the Cancer Moonshot℠ at a future BSA meeting.

- Dr. Lowy remarked that one of the key features of the Cancer Moonshot℠ was the use of cooperative agreements (U funding mechanism), may have partly contributed to the low funding rates for R01s. A detailed report on the RPG Pool and R01s will be forthcoming.

- BSA members suggested exploring cost-sharing mechanisms with other NIH Institutes and Centers to increase funding for cancer research that extends the RPG awards.

- Aside from the MERIT Award, another option to consider is increasing support for traditional R01s that are high scoring, but fall just below the fundable payline, especially in the category of childhood cancer grants.

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

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the new Congress and committee changes, budget and appropriations, and other legislation of interest. Ms. Holohan noted that aside from the leadership changes, several members are new to the Appropriations Committee and L-HHS Subcommittee, and four members of the 115th Congress are no longer serving. No changes were made to the Senate Appropriations Committee and L-HHS Subcommittee. The NCI hopes that this continuity will retain priorities and interest in childhood cancer, disparities research, and electronic cigarettes. Ms. Holohan called attention to the leadership of the committees that authorize NIH funding— the House Energy and Commerce Committee and Health Subcommittee and the Senate Health, Education, Labor and Pensions Committee. These committees authorize the NIH annual appropriations to fund specific programs, which may have specific directions attached. Dr. Lowy will accompany Dr. Francis S. Collins, Director, NIH, and other Institute and Center Directors to the L-HHS Appropriations Subcommittees budget hearings in April 2019.

Ms. Holohan reminded BSA members that on 28 September 2018 the FY 2019 Defense and FY 2019 Labor-HHS spending bill was signed into law, which included a $2 B increase for the NIH, a $79.3 M increase for the NCI, and $400 M for the Cancer Moonshot℠. The White House Office of Management and Budget released its funding requests on 11 March 2019, and the President's proposed FY 2020 budget was released on 18 March 2019. The FY 2020 proposed budget includes a 14.6 percent decrease in funding for the NCI and $50 M appropriation for the Pediatric Cancer Initiative. Agency budget hearings are in progress. U.S. Department of Health and Human Services (HHS) Secretary, Mr. Alex M. Azar, testified at three budget hearings the week of March 11, 2019; the House Energy and Commerce Committee on 12 March 2019; House L-HHS Appropriations Subcommittee on 13 March 2019; and Senate Finance Committee on 14 March 2019. Ms. Holohan noted some challenges regarding the FY 2020 budget: The debt ceiling was reinstated on 1 March 2019, and the budget caps (defense and non-defense) will return on October 2019. Congress will need to decide on new budget cap levels for discretionary and nondiscretionary accounts, pass legislation to extend the deadlines, or vote to suspend the debt limits.

Ms. Holohan noted other legislation of interest to the NCI. The Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act was signed into law in June 2018 and includes provisions encouraging action from the HHS, NCI, and the Centers for Disease Control and Prevention and requiring reporting. Four sections of the STAR Act pertain to the NCI and NIH: *Section 101*, Children's Cancer Biorepositories and Biospecimen Research; *Section 111*, Inclusion of at Least One Pediatric Oncologist on the NCAB; *Section 112*, Sense of Congress Regarding Pediatric Expertise at the National Cancer Institute; and *Section 202*, Grants to Improve Care for Pediatric Cancer Survivors. NCI's implementation activities for the STAR legislation are underway. A funding opportunity announcement (FOA), RFA-CA-19-033-Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors, was released on 11 January 2019. The first application receipt date was 15 March 2019, and a second receipt date will be 3 January 2020. In May 2019, the NCI will convene a meeting with pediatric cancer researchers, biospecimen science experts, research organizations, and advocates to discuss scientific challenges related to pediatric biospecimen collections.

IV. REPORT ON TISSUE BANKING ACTIVITIES ACROSS THE NCI: THE APPROACHES AND REACH TO THE CANCER RESEARCH COMMUNITY —DR. LYNDSAY HARRIS

Dr. Lyndsay Harris, Associate Director, Cancer Diagnosis Program (CDP), Division of Cancer Treatment and Diagnosis (DCTD), provided an update on the NCI biospecimen resources (BSRs) and began with the main messages from the landscape assessment survey. BSRs are historically diverse; may serve basic, translational, and clinical investigators; and are supported by individual grants, cooperative agreements,

contracts, or intramural funds. Resources have been developed for the Cancer Centers, Specialized Programs of Research Excellence (SPOREs), NCTN, and the Division of Cancer Control and Population Sciences (DCCPS) and Division of Cancer Epidemiology and Genetics (DCEG) high-risk cohorts. Each BSR adheres to resource-specific standard operating procedures for specimen collection and distribution; maintains and manages a biorepository; and varies in the type of specimens (e.g., cell lines and/or frozen tissue) collected. The resource information technology (IT) systems follow the course of specimen collection, storage, and distribution and make provision for specific resource goals and needs of the investigator. The review and re-assessment of resources to re-issue the infrastructure grants occur every funding cycle.

Dr. Harris described the NCI BSR survey questions and noted that the responses reflect only specimens collected and distributed in 2017. Several BSRs had higher distributions in other years that were not evaluated. The results identified 44 NCI-supported BSRs: three in the Office of the Director (OD), five in DCTD, four in the Division of Cancer Biology, 18 in DCCPS, four in DCEG, six in DCP, one at the Center for Cancer (CCR), and one DCEG/DCP shared resource. Biospecimen access can be public, controlled, or collaborative. The Cooperative Human Tissue Network (CHTN) is a public access only resource available to the extramural community. In 2017, roughly 1,100 investigators accessed the CHTN and the research generated more than 850 publications over the last 5 years. Fifty-nine Cancer Centers and 52 SPORE supported programs responded to the survey, and access is restricted to members of the scientific networks. Priority is given to specific ongoing research project investigators for the DCCPS, and DCEG specimens and are made available to other investigators after a project completes. The NCI intramural investigators and their collaborators are the primary customers of the CCR, DCEG, OD, and Clinical Proteomic Tumor Analysis Consortium (CPTAC) specimens.

Dr. Harris detailed specific collections and distributions from NCI Divisions and programs that had been completed in 2017. In the DCTD, the CHTN collected 50,000 specimens and distributed 44,259. The NCTN Banks collected 351,177 specimens and distributed 104,501. The ETCTN, which is one of the newer banks, has not distributed any specimens to date. The SPOREs collected 169,484 specimens and distributed 22,962. The Genotype-Tissue Expression (GTEx) bank, an organ donor repository, has completed its collections and distributed 8,775 specimens. In the DCPPS and DCEG, 1,250 specimens were collected within the 18 epidemiology cohorts and 11,000 were distributed. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial bank collected 11,450 specimens and distributed 88,454. The intramural principal investigator bank collected 189,831 and distributed 144,992. In the CCR, the Blood Processing Core collected 29,008 specimens and distributed 7,817. The Clinical Pathology Archives/Anatomic Pathology bank collected 19,626 specimens and distributed 16,491. The Clinical Pathology Archives/Tissue Procurement and Processing Facility collected 310 specimens and distributed 15.

Dr. Harris reminded BSA members that the cooperative agreement grants (U grants) support BSR infrastructure, including specimen collection, processing, storage, and distribution for research. As an example, the NCTN Banks are Resource-related Research Projects funded via the U24 mechanism. A unique resource, the five NCTN Banks collectively store and provide researchers with well-annotated specimens and clinical data from NCTN trials, and specimens are used for integral and integrated biomarker studies and assays. Any specimens remaining after clinical trial requirements have been met are considered legacy specimens and are made available to investigators for correlative studies after an established access and approval process managed via the NCTN Navigator. From 2013 to 2017, 1.75 million tumor specimens were collected in the NCTN Banks, and the research has resulted in 572 publications. The NCTN Navigator, a web-based clinical specimen and data resource, launched in April 2018. As of October 2018, published data from 105 clinical trials had been loaded, which includes 57,550 patient cases and 654,160 specimens. Further details on NCI BSRs can be accessed from the NCI Research Resources, Specimen Resource Locator, and DCTD and CDP websites. Communication efforts

to inform the scientific research community about the NCI BSRs include presentations at national meetings, the NCI CDP email to NIH grantees, and GovDelivery (a government platform for public subscribers) emails.

In the discussion, the following points were made:

Program staff clarified that the Cancer Center Support Grant (CCSG) and SPORE-funded programs, which are required to maintain biospecimen cores, were represented in the survey results as aggregates, rather than individual resources. Those data can be provided to the BSA.

- Establishing uniformity across the NCI BSRs is a goal the NCI should consider because the resources serve the whole cancer research community. Although no central IT system can currently accommodate all the NCI BSRs, certain commonalties could be harnessed to confer uniformity across resources/banks. Leveraging the Cancer Moonshot℠ National Cancer Data Ecosystem model of interoperability would be one place to begin.

- NCI consideration should be given to establishing a minimum biospecimen collection standard and essential data elements for NCI BSRs and leveraging the expertise of the CCSG- and SPORE-funded programs. These approaches would ensure diverse racial and ethnic representation in the specimen collections.

- Searchability and/or uniformity enhancements to existing biospecimen banks should also be considered. However, given the current RPG Pool funding limitations, these features could add to the CCSG "unfunded mandates."

- Supporting one-time administrative supplements to existing BSR sites to maximize their interface with the NCTN Navigator or similar clinical trials resource locators would be helpful.

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

Division of Cancer Control and Population Sciences (DCCPS)

Cancer Intervention and Surveillance Modeling Network (CISNET) (Clinical Trials Not Allowed) (Re-issue RFA/Coop. Agr.)—Dr. Eric Feuer

Dr. Eric Feuer, Chief, Statistical Methodology and Applications Branch, Surveillance Research Program, DCCPS, presented the re-issue concept for CISNET, a consortium of NCI-sponsored statistical modeling investigators. Dr. Feuer stated that, formed in 2000, CISNET is a sponsored collaborative of the simulation of six cancer sites: breast, prostate, colorectal, lung, esophagus, and cervical. The purpose is to extend evidence provided by clinical trial, epidemiologic, and surveillance data using simulation modeling to guide public health research and priorities. CISNET holds a unique niche in the NCI portfolio to address the gap between the rapid pace of cancer research innovation and the research community's ability to efficiently harness those innovations to improve population health. Individual modeling efforts can yield inconsistent results, which often are challenging to interpret. An approach innovated by CISNET—comparative modeling—is a systematic process in which central questions are addressed collaboratively by modeling groups based on a common set of inputs/outputs in the CISNET model framework. Each of six multiple principal investigator–led modeling groups, at six different institutions, focuses on one specific cancer site. A cancer site–specific coordinating center oversees the data collections and operations. Affiliate members may join on specific collaborations.

Dr. Feuer informed members that an overarching goal of CISNET has been outreach and collaborations with many different groups and consortia on ways that modeling can assist in responding to questions difficult to answer by any other means. Since 2000, more than 450 CISNET peer-reviewed papers have been published. Of the 450, 40 per year were published in the current funding cycle; 50 percent were published in journals with impact factors of 5 or higher; and 25 percent in journals with impact factors higher than 15. CISNET modeling has provided policymakers with estimates of the benefits versus harms of screening regimens and increased understanding into the impact of advances in treatment and screening on population mortality trends. In 2014, CISNET investigators simulated more than 500 screening regimens to support extrapolating data from the single National Lung Screening Trial (NLST) regimen to inform the U.S. Preventative Services Task Force guidelines. The contribution of advances in mammography, chemotherapy, hormonal therapy, and target therapy to the decline in U.S. breast cancer mortality was quantified using CISNET modeling and reported on in 2005 and 2018.

The re-issue RFA will support continuing the CISNET six cancer modeling sites and cross-program activities, including the ongoing collaborations, and establishing the Junior Investigators Career Enhancement (JUICE) program. The applications should address the ongoing priorities to focus the modeling efforts and opportunities exist for modeling precision treatment.

Subcommittee Review. Dr. Melissa L. Bondy, Professor and Associate Director, Department of Medicine, Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, expressed the Subcommittee's strong enthusiasm for the concept re-issuance. The Subcommittee agreed that CISNET has been a valuable, productive, and successful network, which has expanded over the four funding cycles. The Subcommittee noted that establishing the JUICE program will be a worthwhile asset to the network. However, the NCI should clarify in the RFA that applicants need to address only one of the nine priority areas.

In the discussion, the following points were made:

- Program staff clarified that cancer site priorities will be sorted into categories relative to scientific objectives and aligned with the external review recommendations.

- The NCI could consider accepting applications from external groups and junior investigators that address the CISNET crosscutting themes and/or global modeling issues.

The first year's cost for the one-time issuance is estimated at $10 M for 6 U01 awards, with a total cost of $50 M for 5 years.

Motion. A motion to concur on the re-issuance of the Division of Cancer Control and Population Sciences' (DCCPS) RFA/(Cooperative Agreement [Coop. Agr.]) (Clinical Trials Not Allowed) entitled "Cancer Intervention and Surveillance Modeling Network (CISNET)" was approved with 22 ayes, zero nays, and 1 abstention.

VI. ONGOING AND NEW BUSINESS—DR. DAFNA BAR-SAGI

Establish an *Ad Hoc* Working Group on Prevention. Dr. Bar-Sagi stated that the Board will need to concur on establishing an *ad hoc* Working Group on Prevention. The goal, charge, and mission statement have been provided in the Board book. Dr. Sharpless commented on the changing nature of cancer prevention and noted that the NCI DCP has a research portfolio that focuses on early diagnosis and screening, but not solely on prevention. The aim is to convene traditional cancer prevention/screening researchers and non-traditional cancer prevention thought leaders to advise the NCI on opportunities and

ways of modifying its prevention research portfolio. The Working Group would be addressing a clear need for the NCI, and its activities will run parallel to the search for a new DCP Director.

In the discussion, the following points were made:

- The Working Group will take a futuristic look into prevention and early screening opportunities across the NCI. However, it will not necessarily focus on a DCP portfolio analysis.

- Similar to the NCAB Small Business Innovation Research (SBIR) and Global Health Working Groups, the Prevention Working Group could potentially make recommendations on future funding opportunities and overall structure of a prevention program, as well as making statements about diversifying the NCI cancer prevention research portfolio.

Motion. A motion to concur with establishing a BSA a*d hoc* Working Group on Prevention was approved unanimously.

BSA Consideration of Program Announcements with Special Receipt, Referral, and/or Review (PARs). Dr. Gray informed BSA members that the NIH has indicated that PARs are to be discussed by a body convened under the auspices of the Federal Advisory Committee Act (FACA) at a meeting open to the public and that the BSA has been designated as that body.

Regarding PARs and Notices, new concepts will be assigned to three BSA members, using the same process that is in place for RFAs and research and development RFPs. Program directors of new concepts will be encouraged to contact the assigned reviewers to see if there are issues or concerns. The difference between PARs and RFAs is that no monies are set aside. Thus, the discussion during the meeting will focus only on the science. Following staff presentations, the assigned members will be asked to provide their comments, and the full Board will discuss the concept. A vote to approve, disapprove, or defer must be taken. If the concept is deferred, the concept will be presented at a future BSA meeting. Only Notices with dollars attached (e.g., competitive or administrative supplements) will come to the BSA. Due to the large volume of approximately 60 PAR re-issues annually, these will be considered for review as a group, not individually. The Board will be sent a listing of all re-issues and will be asked if there are issues/concerns. If any issues are shared by a majority of the BSA members, program staff will be available at the full Board meeting to respond. The Board will vote en bloc to concur with the re-issuances. The name of each concept will be listed in the minutes. The process for new and re-issue Notices will be handled similarly.

Dr. Gray requested BSA concurrence for indefinite re-issuance of select PARs. Those PARs are: 1) training initiatives (regular and diversity) – specifically, Career Development (Ks), Research Education (R25s), and Predoctoral Fellowship (F31), i.e., the Ruth L. Kirschstein National Research Service Awards for Individual Predoctoral Fellowships to Promote Diversity in Health-Related Research; 2) Small Research Project (R03)-Omnibus; 3) Program Project (P0l); 3) SPORE (P50); and, 4) CCSG (P30). She noted that these PARs will, however, require BSA concept concurrence when there are major changes in the FOA.

In the discussion, the following point was made:

- PARs are funded from the RPG Pool and are peer reviewed and scored accordingly.

- The FACA rules governing BSA external discussions on RFAs also apply to the PARs.

Motion. A motion to approve the BSA concurrence for indefinite re-issuance of select PARs was approved unanimously.

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

Office of the Director

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

Dr. Mostafa Nokta, Director, AIDS Cancer Clinical Program, Office of HIV and AIDS Malignancy (OHAM), presented a re-issue concept for the AMC, an NCI-supported clinical trials group. Dr. Nokta reviewed the state of the HIV epidemic, which continues to be a public health problem. At the end of 2017, it was estimated that approximately 36.7 million people were living with HIV worldwide, and approximately 1.8 million new cases are being diagnosed annually. Of the 1.8 million annual new cases, 50 percent are women. In the United States, 1.1 million people live with HIV; in sub-Saharan Africa, 19 million; and in Latin America, 2.3 million. Cancer has been a prominent manifestation of HIV/AIDS since the beginning of the epidemic and is a leading cause of morbidity and mortality in people living with HIV (PLWH).

Dr. Nokta explained that non-Hodgkin's lymphoma and Kaposi sarcoma (KS) remain the leading AIDS-related cancers in PLWH in the United States; non-AIDS defining cancers (e.g., lung, anal, liver) are a close second. In Africa and other developing countries with limited access to antiretroviral therapy (ART), AIDS-defining cancers continue to be the overall cancers observed in PLWH. The incidences of KS, cervical cancer, and other viral-related cancers are higher in African countries, and KS is more common in men. In addition, cervical cancer is the second most common cancer in women in low- and middle-income countries. The AMC was established in 1995 to address the heavy burden of HIV-associated cancers worldwide. Its fourfold mission is to develop and evaluate clinical interventions for the treatment and prevention of malignancies in PLWH; conduct Phase I, II, and III clinical trials of HIV-related malignancies; investigate the biology of HIV-related malignancies in the context of clinical trials; and contribute specimens and clinical data to the AIDS and Cancer Specimen Resource.

The AMC is composed of an Executive Committee, an Administrative Office, five Working Groups, a Statistical Office, an Operations and Data Management Office, and 36 clinical trial sites worldwide. In the current funding cycle, AMC investigators developed 15 protocols, completed enrollment on 14 protocols, and accrued 2,887 patients into clinical trials; 14 protocols are actively accruing patients. There were 39 publications in peer-reviewed journals during this period. To date, the largest AMC trial—Anal Cancer High-grade Squamous Intraepithelial Lesions [HSIL] Outcomes Research (commonly called ANCHOR) Study—has screened more than 7,000 participants and randomized 2,804 for treatment. Dr. Nokta highlighted numerous other AMC accomplishments since the last renewal, including therapeutic approaches, training, feasibility studies, and clinical practice–changing methods.

A 2018 mid-cycle program evaluation identified several strengths in support of the concept re-issuance and proposed recommendations that the AMC began to rapidly address. This re-issuance RFA will support increasing enrollment into U.S.-based AMC trials, conducting international trials, and addressing current scientific needs, including optimizing standards of care for progressive cancers and optimizing treatment in resource-limited countries.

Subcommittee Review. Dr. Leslie L. Robison, Chairman, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Associate Director, St. Jude Comprehensive Cancer Center, expressed the Subcommittee's support for the re-issue concept, noting the unique and underserved population being addressed within the cancer spectrum. The AMC's overall productivity, especially in

terms of practice-changing methods, has been significant. Dr. Robison noted that 1) the U.S.-based NCI Clinical Trials Cooperative Groups have expanded participant eligibility to include PLWH and might warrant a discussion within the NCI on the impact to AMC clinical trial accruals; and, 2) that the need to shorten the protocol development period is important for the AMC, and any requirements (e.g., length of time) should be highlighted within the RFA. Although monitoring and performance measures for assessing trial enrollment are in place, as well as a financial model, Dr. Robison indicated that the Subcommittee expressed concern that the re-issue RFA plans for accruals may not be clear across the AMC.

In the discussion, the following points were made:

- The AMC leadership takes the issue of trial accrual seriously and frequently convenes meetings to discuss barriers, challenges, and strategies. In fact, outreach efforts to high disease burden areas are being planned. Some of the non-AMC ANCHOR sites are being converted to enroll patients. Streamlining the protocol development process is expected to shorten the time from inception to activation, resulting in more open trials. A new executive officer was recently recruited to oversee trial enrollment at the AMC sites and to identify local issues.

- Per the external review recommendations, the opportunity exists to expand the AMC to include cancer prevention and survivorship studies.

- NCI-appropriated AIDS funds, as established by the NIH Office of AIDS Research, will support this research initiative.

- A memorandum of understanding was recently signed between the NCI and the international organization, Unitaid, to conduct cervical cancer screening clinical trials in both women who are HIV positive and those who are HIV negative. This effort leverages the Cancer Moonshot℠ prevention and early detection initiatives, and if successful, could result in changes to the standard of care for women with HIV.

The first year's cost for the one-time issuance is estimated at $24 M for one UM1 award and three R21 awards, and $22.7 M in years 3–5, with a total cost of $116.2 M for 5 years.

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

Division of Cancer Treatment and Diagnosis

Cancer Trials Support Unit (CTSU) (Re-Issue RFP)—Ms. Shanda Finnigan

Ms. Shanda Finnegan, Associate Branch Chief, Clinical Trials Operations and Informatics Branch, DCTD, described the CTSU re-issue RFP concept. Ms. Finnegan noted that this is the first year the CTSU is being reviewed by the BSA in light of a change in the NCI policy. The CTSU, which was established in 1999, is a research support contract, not a research contract. In supporting clinical trial management and conduct for the NCI, the CTSU is integral to the NCI's clinical trials conduct and infrastructure. It provides services for the NCTN, ETCTN, NCI Community Oncology Research Program (NCORP), and other smaller networks (e.g., Adult and Pediatric Brain Tumor Consortia, Cancer Immunotherapy Trials Network, and the Pediatric Early Phase Clinical Trials Network). The objective of the CTSU is to provide centralized operational support during the full lifecycle of clinical trials. This support is multifaceted and involves facilitating research staff participation in NCI programs and trials, providing standardization and integration of processes, identifying best practices, and improving the operational efficiency of the

clinical trials system. In recent years, the CTSU has focused on enhancing services to accommodate the needs of cancer prevention trials, including the NCORP's Community Sites and Minority/Underserved Community Sites, and the Cancer Care Delivery Research (CCDR) Program.

Regarding the scope, the CTSU offers 24/7 operational support for the entire lifecycle of the clinical trial. Eighty-seven percent of actively enrolling treatment trials currently use the CTSU, including more than 95 percent of newly activated treatment trials and 100 percent of newly activated NCTN and ETCTN treatment trials. The CTSU currently supports a grant portfolio of approximately $343 M annually. To date, the CTSU has supported more than 300 Phase III clinical trials on annual budgets of $23 M, which is a significant return on NCI investments compared with the average cost of $23.1 M of conducting one industry-sponsored Phase III trial. Ms. Finnegan pointed out that enthusiasm within the NCI clinical trials groups for the CTSU has grown over the past 20 years, communications across the groups has improved, and true partnerships have been established. The NCI leadership saw the potential in the CTSU from the beginning and has continued to support the CTSU both publicly and with funding.

Ms. Finnegan detailed the CTSU enrollment process. In the pre-enrollment stage, the CTSU aims to reduce the amount of time required to accrue patients to trials by integrating institutional review board (IRB) approvals with a centralized IRB (CIRB) and streamlining access to study documents. Electronic medical record (EMR)-enabling capabilities are being built, and a concise spreadsheet to summarize pertinent information about a study is available on the CTSU website via a credentialed access system. A streamlined process for subject enrollment with multiple checks to ensure Good Clinical Practice compliance has been developed. All sites utilize the Oncology Patient Enrollment Network (OPEN) for all patient enrollments. For enrolled subjects, the CTSU has a multifaceted data quality support system. Users have a standardized data portal, regardless of which organization leads the study. Data input to OPEN is imported into Medidata's Rave® (Rave), a standardized clinical data management system. Rave allows the CTSU to track, monitor, and audit patient data. Targeted source data verification allows results from some data fields to be checked and captured in Rave. Remote and in-person auditors have standardized access and training. The data quality portal and source document portal provide easy access and data management for all studies in Rave. A performance assessment score for sites currently is under development.

In 2018, the CTSU accrued 40,451 subjects, for a total of 180,565 throughout the course of the contract. There are 21,348 CTSU website staff and services are provided to 17,688 investigators online. Currently, 587 protocols are posted to the CTSU website, which receives on average 85,548 visits per month. IRB approvals average 21,391 per month. The Data Quality Portal Data Warehouse currently has more than 150 million records. The help desk averages 1,893 inquiries per month. The CTSU has completed 157 national coverage analyses (NCAs) for Medicare and Medicaid. Ms. Finnegan reviewed the CTSU's accomplishments. The CTSU's adoption of the Rave system has standardized integration across networks. The CTSU has supported precision medicine trials, implemented the NCTN Navigator, instituted a single database to record adverse events, supported increased regulatory compliance, and provided ongoing site support for EMRs and NCAs. This RFP re-issuance will support continuing optimizations and integration of CTSU services to further increase efficiency. The CTSU also will focus on optimizing the operations of the EMR and NCA, which will significantly decrease the administrative burden on local sites.

Subcommittee Review. Dr. Keith T. Flaherty, Director, Henri and Belinda Termeer Center for Target Therapy, Director of Clinical Research, Massachusetts General Hospital Cancer Center, expressed the Subcommittee's support for the RFP-re-issue concept. Dr. Flaherty underscored that building the EMR capability is a very important priority. The Subcommittee expressed that the CTSU is efficiently run and less expensive than corporate pharmaceutical equivalents.

In the discussion, the following points were made:

- Program staff clarified that 120 contract staff support the CTSU's day-to-day operations and that a few NCI staff are assisting.

- Approximately 50 percent of patients accrued to the CTSU in the past contract year were NCTN-registered patients.

- The CTSU is working to modify OPEN to account for the changes in how CCDR studies are performed. Changing OPEN requires extensive time to account for its many interrelated components.

The first year's cost for the one-time issuance is estimated at $23 M, with a total cost of $230 M for 10 years.

Motion. A motion to concur on the Division of Cancer Treatment and Diagnosis's re-issue request for proposal (RFP) entitled "Cancer Trials Support Unit (CTSU)" was approved unanimously.

Office of the Director

Small Business Innovation Research (SBIR) Contract Topics (New RFP)—Dr. Andrew Kurtz

Dr. Andrew Kurtz, Program Director and Team Leader, SBIR Development Center, introduced the RFP concept for 16 contract topics proposed for new SBIR awards in FY 2020. The technical scope of these topics is defined by an NCI concept review process. New topics are selected once per year. Due to a recent NCI policy change, this is the first set of SBIR contract topics being reviewed by the BSA. The NCI evaluates topics in terms of how well they address NCI technology priorities, whether the proposed research and development is appropriate for small businesses and has commercial potential, how well the topics address gaps in the NCI portfolio, and the extent to which they align with other NCI programs. The 16 topics proposed for FY 2020 are within three major categories: therapeutics, clinical diagnostics and molecular analysis, and information technology and bioinformatics.

Dr. Kurtz described the 16 SBIR FY 2020 topics, including the goals and project requirements and noted that the SBIR contract topics align with the Cancer Moonshot℠ NCAB Blue Ribbon Panel (BRP) recommendations and crosscutting themes. Detailed reports have been provided in the Board book.

Therapeutics Topics

Manufacturing Innovation for the Production of Cell-Based Cancer Immunotherapies. Improve, modernize, and accelerate commercial-scale manufacturing of cell-based immunotherapy products. Projects will be expected to show clear improvements in manufacturing using at least one cell-based product that represents a particular class of therapy.

Development of Senolytic Agents for Cancer Treatment. Conduct preclinical development of novel anti-cancer agents that selectively target senescent cells, which accumulate in aging tissues. Projects will be expected to address well-validated molecular targets and to use accepted markers of senescence to show selective cell-killing preclinical models.

Combinatory Treatment Modalities Utilizing Radiation to Locally Activate or Release Systemically Delivered Therapeutics. Conduct preclinical development of novel agents or drug formulations that can

be activated upon treatment with ionizing radiation. Projects will be expected to develop agents that can be tested and deployed in clinics that already contain existing infrastructure to deliver ionizing radiation.

***Sensing Tools to Measure Biological Response to Radiotherapy*.** Develop either *in vitro* or *in vivo* sensors that provide biological response information that would complement the physical radiation dose information. The sensors should provide both spatial and temporal information for appropriate biomarkers or pathways to give a biological reading of a tumor or its micro-environment.

Clinical Diagnostics and Molecular Analysis Topics

***Quantitative Biomimetic Phantoms for Cancer Imaging*.** Develop and validate imaging phantoms made from materials that best represent the unique characteristics of organs commonly afflicted with cancers. Projects are expected to incorporate reference standards into the biomaterials (e.g., imaging agents) to calibrate the phantom device for quantitative analysis.

***Artificial Intelligence–Aided Imaging for Cancer Prevention, Diagnosis, and Monitoring*.** Develop image analysis software aided by artificial intelligence to assist physicians with clinical decision making. Projects can focus on analyzing data from a single modality or a combination of modalities, depending on the clinical question that the tool is intended to answer.

***Spatial Sequencing Technologies with Single Cell Resolution for Cancer Research and Precision Medicine*.** Develop new technologies that generate sequence information from tissue slides without losing the histological context of the gene targets. Projects will be expected to use either native tissue or organoid specimens, with a near-term goal of developing commercially available research tools and a long-term goal of leveraging these technologies to develop new cancer diagnostics.

***Subcellular Microscopy and 'Omics in Cancer Cell Biology*.** Develop new technologies, providing spatially resolved, molecular phenotype information by integrating high-resolution microscopy with single-cell 'omics approaches. Non-sequencing-based approaches will be solicited.

***Intra-Tumor Sensing Technologies for Tumor Pharmacotyping*.** Develop sensing approaches that provide *in vivo* readouts on the efficacy of candidate therapeutic agents within solid tumors.

Information Technology and Bioinformatics Topics

***IT Tools to Improve Patient Navigation Through the Cancer Care Continuum*.** Develop tools that assist decision making and reduce the burden of tasks completed by patients and patient navigators.

***Cloud-Based IT Tools for Big Data Analysis in the Cancer Research Data Commons (CRDC)*.** Develop new or existing analytic tools that provide secure access to various big data types within the CRDC. Engage the private sector to develop commercial analytic tools that can be broadly disseminated and sustained within the cancer research community.

***Tools and Technologies for Visualizing Multi-Scale Data*.** Develop tools that enable integration, visualization, and analysis of data generated using different assays and analytical approaches. Projects will be expected to integrate data that are relevant to programs developing health and disease atlases.

***IT Tools for Automated Analysis of Physical Activity, Performance, and Behavior from Images for Improved Cancer Health*.** Develop software that can automatically extract physical activity data from patient images or videos for clinical and home monitoring. The tools must protect any sensitive or personally identifiable information that could be obtained from the acquired images.

Cancer Clinical Trials Recruitment and Retention Tools for Participant Engagement. Develop tools for clinicians and participants that address barriers to participation, simplify recruitment, and increase retention. Projects are expected to involve web-based tools, social media, patient registries, and databases to increase recruitment and retention and to improve education and patient engagement in a culturally sensitive manner.

De-Identification Software Tools for Cancer Imaging Research. Develop tools that automate the removal of protected health information from image data files to facilitate data sharing. Projects will be encouraged to develop tools for computed tomography image files and digital pathology images.

Software Enabling Data Integration from Wearable Sensors to Generate Novel Analytics for Cancer Patients. Develop software that can integrate objective data from wearable sensors to support clinical cancer research. The software should be utilizable across multiple data types and sources and compatible with existing passive and continuous monitoring devices.

Subcommittee Review. Dr. Martine F. Roussel, St. Jude Children's Research Endowed Chair in Molecular Oncogenesis, Co-leader of the Cancer Biology Program in the St. Jude Comprehensive Cancer Center, Full Professor, Department of Molecular Sciences, The University of Tennessee, Full Member, Department of Tumor Cell Biology, St. Jude Children's Research Hospital, expressed the Subcommittee's strong support for the concept and noted that the NCI staff presentation addressed the topics' level of overlap with other NCI initiatives. Dr. Roussel remarked that the topics for FY 2020 are interesting and timely, especially the development of new tools in computational biology, IT, and bioinformatics. The overall economic impact of the SBIR program has shown an impressive return on NCI's investment. The Subcommittee indicated that the range of topics well fits the Cancer Moonshot℠ recommendations and other priority initiatives. This concept addresses important problems that can be accomplished by the small-business community.

In the discussion, the following points were made:

- The Quantitative Biomimetic Phantoms (QBP) for Cancer Imaging project may not be commercially viable, and the NCI should consider revisiting the commercialization plan.

- The main rationale in support of QBP is that although the use of phantoms in early-stage imaging studies is very common, the phantoms in the current portfolio are artificial and do not effectively mimic organs. The SBIR Development Center sees the approach detailed in the QBP topic as a better surrogate for actually imaging an organ. These research technologies would be sold to other companies and academics who seek surrogates of human organs for early imaging studies.

- For the topic on wearable sensors, expert panels advise the contractors on which sensors to use. Any type or class of sensor is possible under this topic, such as ones that measure both external contaminant exposures and internal metabolism data.

- BSA members observed that challenges related to clinical trials recruitment, retention, and participant engagement have been discussed multiple times in this meeting, i.e., the AMC, the CTSU, and now the SBIR concepts contract topic. The opportunity exists for implementing mechanisms that encourage coordination and collaboration across the NCI programs and initiatives. Staff noted that for the clinical trials recruitment, retention, and participant engagement topic, the SBIR Development Center is soliciting companies to provide solutions in the form of tools and a business model.

- The SBIR Development Center's Technology Advisory Groups consider the state of the industry when deciding upon contract topics, including whether larger industry players already have a position in a certain technology. The Development Center attempts to identify gaps in existing technologies. It also considers that some technologies developed under SBIR could be acquired by larger companies.

- The demand for patient navigation services is greatly increasing. It once occurred in the early stages of the cancer care continuum. However, it is now expanding into later stages. Electronic tools to assist in patient navigation currently are underutilized.

- Visualization of high-dimensional data is an emerging area in computational sciences, with a goal of translation into the research arena.

- The timeline for success in the SBIR Phase I/II/IIB process is lengthy. The NCI has been using the contract mechanism in earnest only since 2007.

- The Small Business Technology Transfer Research (STTR) mechanism is specifically designed for collaborations between academic institutions and small-business collaborations. STTR statutory requirements mandate that companies partner with nonprofit research institutions, and that at least 30 percent of the work by budget must be performed at the academic institution. Although no official academic requirement exists for SBIR, a significant fraction of SBIR work still goes to academic institutions through collaborations.

- The NCI noted that between 1998 and 2010, 690 Phase II SBIR/STTR grants were awarded to 444 small companies, leading to 247 individual products that have reached the market.

The first year's cost for the one-time issuance is estimated at $10.5 M for 35 N43 awards, with a total cost of $10.5 M for 1 year.

Motion. A motion to concur on the OD's RFP entitled "Small Business Innovation Research (SBIR) Contract Topics" was approved with 22 ayes, zero nays, and 1 abstention.

DCCPS

Clinical Characterization of Cancer Therapy–Induced Adverse Sequelae and Mechanism-based Interventional Strategies (Clinical Trials Optional) (New PAR) —Dr. Kelly Filipski

Dr. Kelly Filipski. Program Director, Clinical and Translational Epidemiology Branch (CTEB), DCCPS, NCI, introduced a PAR concept on the clinical characterization of cancer therapy–induced adverse sequelae and mechanism-based interventional strategies. Dr. Filipski emphasized that little is known about the rates of adverse events that result from new cancer therapies and that several factors currently limit the development of biomarkers, mitigation strategies, and/or prevention strategies. She informed members that the PAR will be a R01 FOA, with clinical trials optional. The PAR will support preclinical and clinical research projects that seek to: 1) clinically characterize adverse sequelae; 2) translate mechanistic understanding into therapeutic approaches to prevent or minimize the development of long-term sequelae; and,, 3) identify mechanisms of new therapy-induced adverse sequelae. Applications are directed to prospectively identify the specific adverse effects or a cluster of effects to be evaluated. Collaborations between clinical and non-clinical investigators are encouraged to couple mechanistic knowledge with the clinical phenotype. Applicants should emphasize translating mechanistic knowledge into approaches or interventions to prevent or mitigate adverse sequelae.

This PAR aligns with NCI Provocative Question (PQ) 9 and the PQ RFAs issued in 2015 and 2017, which examined the mechanism of adverse effects of treatment. The NCI seeks to leverage its investment in the basic mechanistic understanding of these toxicities, coupled with a clinical phenotype, to develop therapeutic approaches to prevent or treat adverse events. A trans-NCI team formulated this PAR, which benefited from each of their unique perspectives. The DCTD seeks to develop and validate new clinical endpoints and biomarkers that can be used in clinical trials and to develop new drugs for the prevention or mitigation of long-term adverse sequelae. The DCP seeks to develop novel agents for evaluation in toxicity mitigation trials, to validate endpoints for use in toxicity mitigation clinical trials, and to clinically phenotype adverse effects, particularly clusters of effects. The DCCPS aims to clinically phenotype for improved capture of toxicity in population studies and to translate new endpoints and biomarkers to improve the quality of life for cancer survivors. The Division of Cancer Biology (DCB) seeks to develop model systems to study the regulation of immune responses affected by cancer therapies leading to adverse sequelae.

Subcommittee Review. Dr. W. Kimryn Rathmell, Cornelius A. Craig Professor, Department of Medicine, Director, Division of Hematology and Oncology, Vanderbilt University Medical Center, expressed the Subcommittee's strong enthusiasm for the PAR concept. The Subcommittee lauded the NCI for its ability to formulate a PAR around a PQ, which is a testament to the success of the PQ program. This PAR will advance knowledge about immune toxicities, in addition to continuing research in chemotherapy toxicities. Subcommittee members remarked that the need is clear for this sequelae research. However, the PAR concept is unlikely to result in new drug development, but it could lead to the repurposing of existing drugs for new therapeutic uses. Since the PAR concept proposes a mechanistic approach to understanding how the adverse symptoms occur, it may lead to innovative strategies to mitigate them.

In the discussion, the following point was made:

- It has been discovered that certain chemotherapy drugs can cause leukemia 5 or 10 years after the drug's administration. Understanding the mechanism(s) is key to addressing such side effects.

Motion. A motion to concur on the DCCPS's PAR (Clinical Trials Optional) entitled "Clinical Characterization of Cancer Therapy-Induced Adverse Sequelae and Mechanism-based Interventional Strategies" was approved unanimously.

VIII. RFA/COOP. AGR. CANCER MOONSHOT℠ CONCEPTS—NEW—NCI STAFF

Office of the Director

Activities to Promote Human Immune-Representing Oncology Models (APHIROM) Initiative (RFA/Administrative Supplement) —Dr. Anthony Dickherber

Dr. Anthony Dickherber, Program Director, Center for Strategic Scientific Initiatives, presented a new concept for promoting the development of human-representing oncology models, which address a new NIH priority. Previous murine models, with humanized immune systems (HIS), have used human fetal tissue to reconstitute human immune systems with varying degrees of success. Existing HIS murine models have various disadvantages that include failure of B cell and monocyte maturation, natural killer and T cell functional impairment, restricted T cell repertoires, high incidences of graft versus host disease, and cost. Dr. Dickherber informed members that the NCI has substantial investments in cancer model development research. In the patient-derived xenograft (PDX) model systems, the most prominent NCI funding investment is the Patient-Derived Models Repository. Other funding mechanisms, such as the

Cancer Engineering Collaborative, Human Cancer Modeling Initiative, Mammalian Models Consortium, SBIR grants, and Innovative Molecular Analysis Technologies Initiative, have funded other oncology models.

Dr. Dickherber stated that the RFA will support new model development to recapitulate innate and adaptive components of the human immune system without the use of human fetal tissue in a manner that provides the most effective models for *in vivo* or *in vitro* immuno-oncology research. The RFA will be responsive to projects that focus on recapitulation of the human immune system using human cells or tissue. Models derived from genetically manipulated immune systems without the introduction of human immune lineage cells will not be considered.

Subcommittee Review. Dr. Kevin Shannon, American Cancer Society Research Professor, Auerback Distinguished Professor of Molecular Oncology, Professor, Department of Pediatrics, School of Medicine, University of California, San Francisco, expressed the Subcommittee's support for the concept. Dr. Shannon remarked that the goals of APHIROM align with the goals of the Cancer Moonshot℠ Initiative. The Subcommittee recognized the need for appropriate experimental models with a recapitulated human immune system to help the emerging field of immuno-oncology research. He indicated that the NCI should ensure that the goal of replacing human fetal tissue is clear in the RFA. The Subcommittee suggested that any models funded should replicate the human immune system and allow human immune cells to grow and mature in a model system, rather than an immunocompetent murine model system.

In the discussion, the following points were made:

- The RFA concept seeks to fulfill the goal that models move away from using fetal tissue, but recombinant murine models could still be useful for immuno-oncology research.

- Recent results showed that human T cell clones were detected living, *ex vivo*, in human tumor tissue after 1 month. These findings should be further examined in study in mouse models and other types of immune-oncology models.

- The pharmaceutical industry views humanized animal models as PDX models, which may not be accurate because different patient donor cells may give different responses.

- The results from humanized animal models may not be representative of human immunological responses because the clinical data to support their use are not available.

- Generating an animal model with a humanized immune system that mimics all characteristics of the human immune system may not be feasible.

The first year's one-time issuance cost is estimated at $1 M for three R33 awards and $1 M for one Administrative Supplement for year 1, with a total cost of $5 M for 4 years.

Motion. A motion to concur on the OD's RFA/Administrative Supplement entitled "Activities to Promote Human Immune-Representing Oncology Models (APHIROM) Initiative" was approved unanimously.

Next Gen Technology for Next Gen Cancer Models (RFA/Coop. Agr.)
—Dr. Daniela Gerhard

Dr. Daniela Gerhard, Director, Office of Cancer Genomics, presented a new concept that involves the use of next-generation technologies for next-generation cancer models (NGCMs). Dr. Gerhard stated that the goal of this RFA concept is to leverage the Human Cancer Models Initiative's (HCMI) NGCMs to identify cancer vulnerabilities. Existing technology has identified hundreds of thousands of cancer-relevant genetic alterations (e.g., as amplifications, mutations, deletions, and translocations), but it remains a challenge to identify which genetic alterations are relevant to the initiation, development, and metastasis of cancer. The aim is to develop reagents and resources and protocols to better understand the essential cancer pathways. In addition, this research will address the issue of patient-specific therapies, which is a well-discussed topic in the cancer research community.

Dr. Gerhard explained that the HCMI is an international consortium, in which the NCI, Wellcome Sanger Institute, United Kingdom, and Hubrecht Organoid Technology, the Netherlands, are partners. The HCMI collections include approximately 1,000 NGCMs, and technologies for model development include organoids and conditionally reprogrammed cells. The HCMI partners decided on a community resource model, and NGCMs are made available to academic and commercial entities via the American Type Culture Collection (ATCC). Molecular characterizations are being completed on the NGCMs, clinical and genomic data are deposited to the Genetic Data Commons (GDC), and protocols used to expand the models can be accessed from the HCMI website. NCGMs of adult (e.g., breast, colorectal, lung) and pediatric cancers (e.g., neuroblastoma) are among the HCMI collections, and the number of cancer types and populations are expanding. To date, 214 U.S. models have been established and are deposited with the ATCC. Efforts to increase minority population representation in the NGCMs include supporting Administrative Supplements through the NCI Center for Health Disparities. The Genomic Assessment Improves Novel Therapy (commonly GAIN) Consortium study is being leveraged to increase pediatric NGCMs. The RFA will support establishing three technology centers and developing standardized reagents, enabling experimental investigations of cancer-relevant questions.

Subcommittee Review. Dr. Sylvia Plevritis, Professor, Department of Radiology and Biomedical Data Science, Co-Chief, Integrative Biomedical Engineering Informatics at Stanford (IBIIS), Stanford University School of Medicine, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Plevritis informed members that the Subcommittee appreciates NCI staff responses to their concerns on the RFA scope regarding the biological and clinical relevance and on the need to address emerging technologies. NGCMs have become quite widespread and may be useful for predictive purposes for individual patient treatment. The accurate use of NGCMs will be helped by the quality assurance/quality control activities to be conducted in studies funded by the RFA. High-throughput screening of drugs with these models would help to advance treatment and research for cancer patients.

In the discussion, the following points were made:

- BSA members agreed that the main issue in the initial review of the RFA was the absence of a scientific or clinical question tied to model development, which has been adequately addressed in the revised RFA. The refined RFA scope clearly links biological questions to the model technology.

- Although establishing a cancer model data commons database would be strategic, the GDC is quite powerful, and data on models are well characterized and will be further enhanced by the development of visualization tools.

- Fifteen NGCMs, currently deposited at ATCC, can be obtained by investigators for research. Efforts were being made to expand the number of NGCMs available to the research community.

The first year's cost for the one-time issuance is estimated at $4 M for three U01 awards, with a total cost of $12 M for 3 years.

Motion. A motion to concur on the OD's RFA/Coop. Agr. entitled "Next Gen Technology for Next Gen Cancer Models" was approved unanimously.

Mechanisms of Cancer Drug Resistance Competing Revisions (RFA)
—Dr. Michael Espey

Dr. Michael Espey, Program Director, DCB, presented a new concept for facilitating studies of the mechanisms of cancer drug resistance using Competitive Revisions. The goal of the RFA is to accelerate the evaluation of new and/or under-explored mechanisms of drug resistance; develop new approaches with classical targets; and promote collaborative efforts that complement the Drug Resistance and Sensitivity Network (DRSN) studies. Established in 2018, the DRSN is a network composed of five disease-specific research centers that conduct studies with the Cancer Therapy Evaluation Program (CTEP) investigational new drug (IND) agents. The CTEP IND agents are a group of more than 60 small-molecule or antibody inhibitors that affect classic oncogenic signaling, epigenetic regulators, and checkpoint targets.

Members were informed that the RFA will support Competing Revision Supplements to extend the work of the DRSN. Competing Revision Supplements are peer-reviewed and support new aims to an existing award. The focus of the supplements is in the areas of mechanistic cancer biology and new models and methodologies in the technology field.

Subcommittee Review. Dr. Karen E. Knudsen, Hilary Koprowski Endowed Professor, Chair, Department of Cancer Biology, Director, Sidney Kimmel Cancer Center, Thomas Jefferson University, expressed the Subcommittee's support for the concept. Dr. Knudsen commented on the widespread enthusiasm in the overall cancer research community for understanding the mechanisms of drug resistance. The Subcommittee indicated support for the RFA since it offers the advantages of uniting with existing programs and giving preference to CTEP IND agents. The Cancer Moonshot℠ goal of addressing mechanisms of resistance to therapies clearly is being met in this RFA. Some of the agents being investigated by the DRSN are not currently FDA-approved therapeutics, which is also a strength of the concept. Allowing non-DRSN investigators to receive revision supplement funding likely will increase the diversity of scientists conducting this type of research. The Subcommittee appreciates NCI staff's providing information on the successes of the DRSN U54 grantees.

In the discussion, the following points were made:

- Current DRSN investigators are eligible for funding, as well other investigators across the NCI portfolio within the programmatic 3-year window. Successfully funded non-DSRN investigators who are awarded revision supplements would be affiliated with the DRSN and participate in their meetings.

  The DRSN network investigators are a very active and collaborative group facilitating cross-fertilization of concepts and reagents.

The first year's cost for the one-time issuance is estimated at estimated at $4.2 M for 10 Competitive Revision Supplements (S1s) for P01s, P50s, R01s, U01s, and U54s, with a total cost of $12.6 M for 3 years.

Motion. A motion to concur on the OD's RFA entitled "Mechanisms of Cancer Drug Resistance Competing Revisions" was approved with 19 ayes, zero nays, and 1 abstention.

IX. ADJOURNMENT—DR. DAFNA BAR-SAGI

There being no further business, the 59th regular meeting of the BSA was adjourned at 4:16 p.m. on Monday, 25 March 2019.

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Date Dafna Bar-Sagi, Ph.D.
Chair, Board of Scientific Advisors

_____ _____

Date Paulette S. Gray, Ph.D.
Executive Secretary, Board of Scientific Advisors