

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

**58<sup>th</sup> Meeting**

**BOARD OF SCIENTIFIC ADVISORS**

**Summary of Meeting**

**March 21, 2017  
Building 31C, Conference Room 10  
Bethesda, Maryland**

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

BOARD OF SCIENTIFIC ADVISORS

MINUTES OF MEETING

March 21, 2017

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 58<sup>th</sup> meeting on Tuesday, 21 March 2017, at 9:00 a.m. in Conference Room 10, Building 31C, National Institutes of Health (NIH), Bethesda, MD. Dr. Chi V. Dang, Director, Abraham Cancer Center, Professor of Medicine, Perelman School of Medicine, University of Pennsylvania, presided as Chair. The meeting was open to the public from 9:00 a.m. until 2:42 p.m. on 21 March for consideration of requests for application (RFAs) and Cooperative Agreements (Coop. Agr.) of new and reissue concepts presented by NCI Program staff and the NCI Acting Director's report.

**BSA Board Members Present:**

Dr. Chi V. Dang (Chair)  
Dr. Dafna Bar-Sagi  
Dr. Ethan M. Basch  
Dr. Michael John Becich  
Dr. Sangeeta N. Bhatia  
Dr. Graham A. Colditz  
Dr. Christopher M. Counter  
Dr. Daniel C. DiMaio  
Dr. Carol E. Ferrans  
Dr. Chanita Hughes-Halbert  
Dr. James V. Lacey  
Dr. Maria Elena Martinez  
Dr. Luis F. Parada  
Dr. Sylvia Katina Plevritis  
Dr. Martine F. Roussel  
Dr. Victoria L. Seewaldt  
Dr. Kevin M. Shannon

Ms. Mary L. Smith  
Dr. David A. Tuveson  
Dr. Kevin P. White  
Dr. Cheryl L. Willman

**Board Members Absent:**

Dr. Kenneth C. Anderson  
Dr. Melissa L. Bondy  
Dr. Arul M. Chinnaiyan  
Dr. Joseph M. DeSimone  
Dr. Karen M. Emmons  
Ms. Diane Zipursky Quale  
Dr. Robert D. Schreiber  
Dr. Ian M. Thompson  
Dr. Cheryl L. Walker  
Dr. Eileen P. White

**Others present:** Members of NCI's Scientific Program Leaders, NCI staff, members of the extramural community, and press representatives.

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### I. CALL TO ORDER AND OPENING REMARKS—DR. CHI V. DANG

Dr. Chi V. Dang called to order the 58<sup>th</sup> regular meeting of the BSA and welcomed current members of the Board, NIH and NCI staff, guests, and members of the public. Dr. Dang 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, in writing and within 10 days, comments regarding items discussed during the meeting. Dr. Dang noted that the future meeting dates are in the Board book.

### II. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI PROGRAM STAFF

#### Division of Cancer Prevention

##### Precompetitive Collaboration on Liquid Biopsy for Early Cancer Assessment (New RFA/Coop. Agr.)

Dr. Lynn Sorbara, Program Director, Division of Cancer Prevention (DCP), introduced a new concept for precompetitive collaboration on liquid biopsy for early cancer assessment. Dr. Sorbara noted that she informed members that this concept aligns with the goals and recommendations of the Beau Biden Cancer Moonshot (Cancer Moonshot). Liquid biopsy, a detection of circulating tumor cells (CTCs) or circulating DNA (ctDNA) in blood, is a non-invasive method of cancer detection that may be used to detect early stage cancer. No standards currently exist for the capture, characterization, and evaluation of liquid biopsy markers for use in screening or early detection of cancer. Dr. Sorbara stated that the purpose of this concept is to (1) establish, with major emphasis on early cancer detection, an NCI public-private partnership program that will promote both development of new technologies and validation of existing

technologies, methods, or assays for identifying and quantifying tumor-associated cells with liquid biopsies; and (2) develop precompetitive alliances with industry to harmonize and validate these technologies.

Dr. Sorbara informed members that recent studies that identify tumor-derived circulating endothelial cells (with liquid Papanicolaou smear) and circulating cancer-associated macrophage-like cells (with CellSieve) hold promise as new targets for liquid biopsy analyses. Despite these advances, technological and biological challenges of using liquid biopsy and CTCs in screening and early cancer detection remain, including low levels of genetic targets and tumor heterogeneity. Liquid biopsy offers an environment with opportunities for precompetitive collaboration on data sharing, data integration, standards, and validations. The intent of the request for application (RFA/ Cooperative Agreement (Coop. Agr.) concept is to encourage applications to address areas where liquid biopsy would be the most beneficial and will focus on three stages: development, harmonization, and application. NCI's other technology-focused programs, Innovative Molecular Analysis Technologies (IMAT) and Small Business Innovation Research (SBIR), have endorsed this concept.

**Subcommittee Review.** Dr. David A. Tuveson, Roy J. Zuckerberg Professor, Director of the Cancer Center, Cold Spring Harbor Laboratory, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Tuveson stated that the Subcommittee understands the need to develop new platforms and new approaches for early detection and monitoring of cancer in patients, but expressed concern with the reproducibility of diagnostics, standardized sample collections, and cross-validation of existing CTC U.S. Food and Drug Administration (FDA)-approved platforms. These methods and platforms are not widely used in the clinical cancer community, and cooperation is lacking between researchers in the few CTC methods that are approved. This concept aims to address these issues and will help to establish precompetitive collaborations and partnerships where cross-validations will be possible and would have support in the private sector. The Subcommittee encouraged the NCI to provide additional oversight to determine whether the outcomes of this precompetitive collaboration provide new ways to stimulate cancer research.

**In the discussion, the following points were made:**

- The RFA/Coop. Agr. should: 1) include established and validated platforms of minimum residual disease or active cancers as appropriate controls for early disease and detection; 2) employ the use of highly validated samples; and, 3) provide compelling evidence of detectable CTCs in the early stages of disease as rationale to support technology development in this area.
- Recognizing that this is a concept to develop technology through a pipeline with appropriate samples, standards, and rigor and that the NCI is leveraging an existing interagency agreement with the National Institute of Standards and Technology to develop standards for ctDNA, it is prudent to ensure that the biology of CTCs is well understood and that the RFA details the conditions or circumstances that afford the greatest success.
- Although the private sector is making large investments in this area, the \$6 million (M) budget for this concept will support synergistic collaboration at the very early stages of development, which would be more effective than the individual efforts of each laboratory. Consideration should be given to doing a cost analysis of clinical validations using a prospective cohort.
- The DCP has expertise in evaluating technology development and is confident that this precompetitive collaboration has high potential for succeeding and will result in new analytically and clinically validated technologies. Technologies that progress to the application stage and early elimination of those that do not meet the rigorous acceptance criteria will be measures of success.

The first year's cost for this one-time re-issuance is estimated at \$6 M for six to eight U01 awards, with a total cost of \$30 M for 5 years.

**Motion.** A motion to concur on the Division of Cancer Prevention's request for applications (RFA/Coop. Agr.) entitled "Precompetitive Collaboration on Liquid Biopsy for Early Cancer Assessment" was amended to include established and validated platforms of minimum residual disease or active cancers as appropriate controls for early disease and detection. The motion was approved unanimously.

#### **U.S.–Latin American–Caribbean HIV/HPV Prevention Clinical Trials Consortium (New RFA/Coop. Agr.)**

Dr. Vikrant Sahasrabudde, Program Director, DCP, presented a new concept for a human immunodeficiency virus (HIV)/human papilloma virus (HPV) prevention clinical trials consortium with Latin America and the Caribbean (LAC). Dr. Sahasrabudde noted that this concept was developed in partnership with NCI's Center for Global Health and the Office of HIV and AIDS Malignancy (OHAM). The goal of the concept RFA/Coop. Agr. is to support partnerships between investigators in the United States and the LAC region to conduct collaborative clinical trials to improve preventative care and reduce the burden of HPV-associated malignancies in high risk HIV-infected individuals. Two high-impact global health epidemics cross-cut this concept: HIV/AIDS, which affects 36 million people worldwide, half of whom are women and most of whom live in low-and-middle income countries (LMIC), such as those in LAC; and, cervical cancer, which accounts for more than a half million cases annually and is prevalent in regions with high incidences of HIV/AIDS—85 percent of the burden of cervical cancer is in LMIC. In the LAC region, two million individuals are living with HIV, the rates of adult HIV prevalence in the Caribbean are second only to that of Sub-Saharan Africa, and the rates in the Latin American region are higher than rates in the United States. The NCI and OHAM's AIDS Malignancy Consortium have supported clinical research on HIV/HPV coinfection focusing on treatment trials, but few trials have focused on prevention, and fewer address the LAC region.

Dr. Sahasrabudde noted that the RFA/Coop. Agr. concept aligns with the 2013 recommendations of the BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy to define optimal methods for screening and prevention of HIV-associated cancers in LMIC and the priorities of the Office of AIDS Research (OAR) fiscal year (FY) 2018 Trans-NIH Plan for HIV-Related Research (Strategic Plan). The NCI will leverage existing U.S. academic and clinical collaborations and the NIH-funded HIV clinical trials infrastructure. Members were informed that the RFA aims to address three research priority areas of HIV/HPV coinfections identified in NCI-led HIV/HPV consultation meetings: optimizing immunosuppression in individuals testing positive for HIV; optimizing, screening, and triage approaches for HIV-positive women; and nonsurgical approaches for HPV-associated precancer treatment in HIV-positive individuals. The concept includes two Specialized Centers, each with three cores: administrative and coordinating core, central pathology and virology laboratory support core, and statistical and data management core. A steering committee will coordinate activities between the two centers.

**Subcommittee Review.** Dr. Maria Elena Martinez, Professor, Department of Family Medicine and Public Health, Program Leader, Reducing Cancer Health Disparities, Moores Cancer Center, University of California, San Diego, expressed the Subcommittee's support for the concept, which meets a high-priority need in the LAC region. Dr. Martinez informed members that the Subcommittee appreciates NCI staff responses to their questions about the burden of disease, the rationale for focusing research on the LAC HIV/AIDS population, scope of research, leveraging existing clinical infrastructure, and type of cancer being addressed.

In the discussion, the following points were made:

- The LAC HIV population may support establishing patient subgroups for conducting clinical trials on immunoprevention and treatment, but establishing a subgroup for screening and triage might be challenging. Leveraging the efforts of the Costa Rica HPV Vaccine Trial is one option to increase the number of patients for screening and triage clinical trials.
- The NCI is encouraged to develop a mechanism for technology development to detect HIV/HPV coinfection, as well as a repository of biospecimens from this initiative that would be made available to the research community.
- Data and resource sharing agreements and requirements differ by country, and the NCI anticipates that the existing and new partnerships between U.S. and LAC investigators will aid in resolving some of these issues.
- The NCI clarified that the Costa Rica HPV Vaccine Trial will give data on the minimum protective dose of vaccine against cervical cancer for HIV-negative patients who are enrolled in the study, but these data are lacking for HIV-positive individuals. This concept will provide some of those answers.
- Training and capacity building are not highlighted in the RFA; it is expected that the partnering groups will address these activities.

The first year's cost for this one-time issuance is estimated at \$4.45 M for two U54 awards, with a total cost of \$22.25 M for 5 years.

**Motion.** A motion to concur on the Division of Cancer Prevention's new RFA/Coop. Agr. entitled "U.S.–Latin American–Caribbean HIV/HPV Prevention Clinical Trials Consortium" was approved unanimously.

### Office of the Director and Division of Cancer Biology

#### Advancing New Enabling Technologies Aligned with the Beau Biden Cancer Moonshot<sup>SM</sup> Initiative (New RFA)

Dr. Jennifer Couch, Program Director, Division of Cancer Biology (DCB), described a concept on advancing new enabling technologies aligned with the Beau Biden Cancer Moonshot<sup>SM</sup> Initiative, a cross-cutting theme of the National Cancer Advisory Board (NCAB) Blue Ribbon Panel (BRP) recommendations. Dr. Couch informed members that the NCI supports technology development across the continuum of research, from concept to dissemination, with major investments in technology-focused programs, including two broad-based initiatives: IMAT and the Informatics Technology for Cancer Research (ITCR) program. She stated that the proposed Cancer Moonshot technology will enter the development pipeline at the Hardening and Validation phase of the process. This initiative will address four technology priority areas: Priority Area A, enhanced experimental and analytical capabilities addressing complexities of cancer development; Priority Area B, new capabilities for advancing precise clinical diagnosis of cancer patients; Priority Area C, novel predictive *ex vivo* and/or *in silico* modeling approaches to accelerate cancer research and development of personalized therapies; and, Priority Area D, new technologies to improve biospecimen and data quality.

Unique to this concept is the focus on technology validation, extensive nonresponsive criteria to screen poorly aligned applications, unique review criteria for significance and approach, and a required

discussion of a “path to implementation readiness.” Applicants will be asked to define performance measures that can be used to substantiate the technical validation for the technology or method proposed. This RFA concept is in response to the 21st Century Cures Act and will be funded via a set-aside of dedicated funds.

**Subcommittee Review.** Dr. Sangeeta N. Bhatia, John J. and Dorothy Wilson Professor, Division of Health Sciences and Technology and Electrical Engineering and Computer Science Institute for Medical Engineering and Science, Koch Institute for Integrative Cancer Research, Brigham and Women’s Hospital, Massachusetts Institute of Technology, informed members of the Subcommittee’s enthusiasm and support for the concept. Dr. Bhatia stated that the Subcommittee expressed concerns about the responsive categories for technology development and the feasibility of including technologies to support biospecimen validations.

**In the discussion, the following points were made:**

- The RFA concept does not specify measures for success and should consider linking study milestones to the funding mechanism to ensure success of the project and a clear path to product commercialization. Also, details on the inclusion of diverse populations and clear measures of a successful product should be included.
- Members encouraged the NCI to provide more clarity on the scope and specifics on the enabling technologies that align with the Beau Biden Cancer Moonshot goals and explain how new technologies and/or leveraging of existing methodologies will be evaluated.
- Although applicants are required only to submit performance metrics that are likely to result in a product useful in the cancer community, and that product does not necessarily have to end in commercialization, technology development for biospecimen validations would probably not lead to commercialization and might be best suited for a cooperative agreement funding mechanism.
- The RFA should include precise details to address the path to implementation readiness. A vision of implementation is not a firm case.

The first year’s cost for this one-time issuance is estimated at \$5 M for 10 R33 awards, with a total cost of \$15 M for 3 years.

**Motion.** A motion to concur on the Office of the Director and Division of Cancer Biology’s new RFA concept entitled “Advancing New Enabling Technologies Aligned with the Beau Biden Cancer Moonshot<sup>SM</sup> Initiative” was approved unanimously.

### **Division of Cancer Treatment and Diagnosis**

#### **Pediatric Early Phase Clinical Trial Network (Re-issue RFA/Coop. Agr.)**

Dr. Malcolm A. Smith, Associate Branch Chief, Pediatric Oncology, Clinical Investigations Branch, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), presented a reissuance concept for the pediatric early phase clinical trial network (PEP-CTN). Dr. Smith stated that NCI’s investments in pediatric phase 1 clinical trials through the Children’s Oncology Group (COG) Phase 1/Pilot Consortium have been productive during the recent funding period, with the conduct of 15 new trials approved by CTEP, evaluations of a range of novel therapies, and effective incorporation of pharmacokinetics and imaging. He noted that the COG Phase 1/Pilot Consortium was renamed the PEP-CTN in recognition of the need for seamless transitions from phase 1 to phase 2 testing for new

agents for childhood cancers, timely source data validation, study monitoring and auditing programs, and studies of targeted agents for specific genomic alterations.

Members were told that the reissuance will support the PEP-CTN, an activity that is distinctive from other clinical trial activities and is a dedicated component that will focus on conducting early phase clinical trials, which will take advantage of new research opportunities in pediatric drug development that are critical to the NCI pediatric drug development program. The PEP-CTN will include an operations and biostatistics core, a core set of institutions, a PEP Agent Prioritization Committee, and central remote monitoring. Eligibility criteria include Medidata Rave® data entry and registration through the Oncology Patient Enrollment Network and the Clinical Trials Support Unit. Evaluation criteria will include the number of early phase clinical trials and pilot studies initiated and successfully completed per year.

**Subcommittee Review.** Dr. Kevin M. Shannon, American Cancer Society Research Professor, Auerback Distinguished Professor of Molecular Oncology, Department of Pediatrics, University of California, San Francisco, informed members that the Subcommittee supports the concept. Dr. Shannon stated that the Subcommittee expressed concerns regarding investments in an imaging core that would be a duplication of current efforts and the issue of competing open trials. The NCI is encouraged to leverage existing infrastructures, such as the Pediatric Brain Tumor Consortium, and develop a repository of samples from patients with known outcomes.

**In the discussion, the following points were made:**

- The RFA should address leveraging the existing infrastructure of NCI's Pediatric Brain Tumor Clinical Trials Consortium to expand clinical trials in the areas of participation and scope (e.g., central nervous system and non-central nervous system tumors with common targets).
- Consideration should be given to: 1) include strategies to reduce the barriers to patient participation in trials (e.g., access to care or socioeconomic status); 2) enhance accrual in pediatric clinical trials; 3) assess the inclusion criteria for young adults in pediatric clinical trials; and, 4) incorporate patient-reported outcomes.

The first year's cost for this one-time re-issuance is estimated at \$4.09 M for one UM1 award, with a total cost of \$20.45 M for 5 years.

**Motion.** A motion to concur on the re-issuance of the Division of Cancer Treatment and Diagnosis' RFA/Coop. Agr entitled "Pediatric Early Phase Clinical Trial Network" was approved unanimously.

### **III. NCI ACTING DIRECTOR'S REPORT—DRS. DOUGLAS R. LOWY, JAMES H. DOROSHOW, AND DINAH SINGER**

Dr. Douglas R. Lowy, Acting Director, welcomed BSA members and attendees to the meeting. Dr. Lowy expressed appreciation to the BSA for their constructive comments in reviewing the concepts and provided an update on the NCI activities. Dr. Lowy was joined by Drs. Doroshow, Deputy Director, Clinical and Translational Research, who provided an update on the NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) trial and the NCI Virtual Drug Formulary, and Dinah Singer, Acting Deputy Director, NCI, who updated the attendees on the implementation of the Cancer Moonshot BRP recommendations.

**NCI Activities.** Dr. Lowy remarked that congressional bipartisan support for the NIH and the NCI remains strong and informed members of a visit by House Appropriators to the NIH and the NCI. He stated that in January 2017, the House Appropriations Subcommittee, consisting of members of Congress

from both parties and Subcommittee Chair, Rep. Thomas Jeffrey Cole, visited the NIH and learned more about the activities of the NCI. The members of Congress attended a presentation at the Cancer Center for Research (CCR) on prostate cancer and learned how a then-experimental and now-commercialized approach increased patient survival. In addition, Dr. Thomas Price, Secretary, U.S. Department of Health and Human Services (DHHS), visited the NIH and the NCI in February 2017. Visiting the CCR, Secretary Price learned how gene therapy was effective in increasing survival in a patient who had been unresponsive to other treatments. Dr. Lowy emphasized that these types of scientific advances in cancer treatment will become more commonplace with NCI's continuing efforts and commitment to cancer research.

**NCI Budget Outlook.** Dr. Lowy informed members that the White House Office of Management and Budget released proposed appropriations for FY 2018, which Congress is working to refine and finalize. Members were told that the NCI is operating under a continuing resolution (CR) that funds the government through April 28, 2017. Two possibilities for the Federal budget past the current CR would be for Congress to either implement a full-year CR or pass an omnibus spending bill for the remainder of FY 2017. Members were reminded that in 2016, the House Appropriations Subcommittee passed a bill to increase funding to the NIH by \$1.25 billion (B) and to the NCI by \$124 M; the Senate Subcommittee on Appropriations passed a bill to increase funding to the NIH by \$2 B and to the NCI by \$216 M. The NCI is allotted more funds from regular increased and sustained appropriations than from appropriations for special initiatives, such as the Beau Biden Cancer Moonshot<sup>SM</sup> FY 2017 \$300 M appropriation, but regular increased and sustained appropriations are necessary to fund different kinds of research. For example, in the past 3 years, the NCI has had to increase funding for new (Type 1) and competing (Type 2) awards by \$100 M per year in the Research Project Grant (RPG) pool to support investigator-initiated research. This increase required a concomitant funding increase for the noncompeting continuation (Type 5) awards. All funding increases described have been achieved, despite fluctuations in the NCI budget. In addition, increased and sustained appropriations from Congress are needed for training new scientists; special projects, such as the RAS Program at the Frederick National Laboratory for Cancer Research (FNLCR); and clinical trials, such as the MATCH trial, which is being supported in the NCI-designated Cancer Centers. The NCI would be challenged to meet its goals without regular increased and sustained appropriations.

**A 1-Dose/2-Dose HPV Vaccine Trial.** Dr. Lowy informed members that the HPV Vaccine Trial being conducted in Costa Rica was reported on at the December 2015 Joint BSA/NCAB meeting and aims to determine whether a single dose of FDA-approved prophylactic HPV vaccines would provide durable protection against cervical cancer. This trial is supported by the NCI and the Bill & Melinda Gates Foundation (Gates Foundation) and is expected to open in mid-2017. Members were told that the data from the pilot studies showed a favorable response and that the NCI meets regularly with the Gates Foundation to discuss progress and status. Dr. Lowy made note of the ongoing activities regarding HPV vaccines, including the February 2017 International Papilloma Virus Conference and the June 2017 NIH-wide meeting, which will include representatives from the Gates Foundation. Parallel clinical trials are being conducted—one in Africa and the other in the United States, which is led by NCI's DCP. In addition, the Gates Foundation and the NCI are jointly supporting serological standardizations to inform future immunologically based non-inferiority vaccine trials. The FNLCR, NCI, will perform these standardizations, and there will be opportunities for regional manufacturers to commercialize the vaccines. These efforts are being coordinated by the World Health Organization (WHO), and the serology standardization reagents will be deposited in a WHO repository in the United Kingdom.

**NCI Virtual Drug Formulary.** Dr. Doroshow informed members that a Virtual Drug Formulary (NCI Formulary), a system established within the NCI that leverages existing mechanisms to provide NCI principal investigators with investigational new drugs (INDs) more rapidly, launched in January 2017 with 15 targeted agents from six pharmaceutical companies. The NCI Formulary has since expanded to include 11 new targeted agents and one additional pharmaceutical company. The investigators or

institutions will hold the license for the INDs. This public-private partnership between the NCI and pharmaceutical and biotechnology companies, organized through Clinical Cooperative Research and Development Agreements negotiated by NCI's CTEP, will expedite clinical trials by reducing the lengthy negotiation process to a 6 to 8-week review cycle for clinical and preclinical study proposals. A clinical Material Transfer Agreement (MTA) between the NCI and the Cancer Centers formalized the expectations of each party. The available agents, participating companies, intellectual property details, applicable forms, and other pertinent information can be accessed on the NCI Formulary website: <https://nciformulary.cancer.gov/default.htm>. Dr. Doroshov emphasized the year-long efforts to establish the formulary and encouraged members to engage their colleagues and Cancer Center investigators to take advantage of this new system.

**NCI-MATCH Trial.** Dr. Doroshov reminded members that the NCI-MATCH trial, coordinated through the Eastern Cooperative Oncology Group and the American College of Radiology Imaging Network (ECOG ACRIN) Cancer Research Group, opened August 2015 with 10 treatment arms or targeted drugs. In a 3-month period, 795 patient tumors were screened (e.g., DNA sequencing to detect gene abnormalities that may be driving tumor growth) for actionable mutations. One thousand approved sites, including 80 percent of Cancer Centers and 90 percent of the NCI Community Oncology Research Program sites, are participating. On average, 115 patients are screened each month, exceeding original estimates of 50 screenings per month. As of 12 March 2017, accrual is more than two-thirds complete, with biopsies of 4,702 patient tumors completed; 20 percent of patients screened (722) were eligible for the trial and 495 have been enrolled for treatment. The genomic analysis success rate is 94 percent, and the median turnaround time for results is 16 days. Although distributions of breast and colorectal cancers of patients enrolled for screening are higher, enrollments of patients with underrepresented cancers in other disease sites has been reasonable over the duration of the trial. As of October 2016, enrollment demographics showed that 80 percent of patients enrolled were Caucasian, 8 percent African American, and 6 percent Hispanic. The distribution of accrual by state was not a direct correlation to a specific population.

Accrual closed temporarily on 11 November 2015, to conduct a built-in interim analysis, and the trial reopened 31 May 2016, with 24 treatment arms; six additional arms were added early March 2017. Seven of the 24 arms have completed accruals and are undergoing initial efficacy evaluations; four others are nearing complete accruals. To address rare cancers that may not otherwise be identified in this phase of the trial, the NCI is working to complete agreements with four additional Clinical Laboratory Improvement Amendments–certified laboratories—including two commercial laboratories, Foundation Medicine Inc. (FMI) and Caris Life Sciences, and two clinical laboratories, M.D. Anderson Cancer Center and Memorial Sloan Kettering Cancer Center—to identify through routine cancer screening for clinical care patients who may have rare driver mutations. This rare-variant initiative, expected to start in May 2017, will verify results from these patients with the MATCH assays retrospectively.

**Implementation of the Cancer Moonshot BRP Recommendations.** Dr. Singer reminded members that then President Barack Obama, in January 2016, announced the Cancer Moonshot and identified three goals: accelerate progress in cancer, encourage greater cooperation and collaboration, and enhance data sharing. The NCI and the NCAB engaged to address these goals by establishing a BRP to develop recommendations of opportunities for the Cancer Moonshot—a report of final recommendations was presented to the NCAB in September 2016. Following the acceptance of the September 2016 Report of the NCAB BRP on recommendations to accelerate the progress of cancer research across the continuum (i.e., basic science, clinical, and population science), the NCI began designing the implementation process to develop funding opportunity announcements (FOAs) for the Cancer Moonshot.

In December 2016, Congress passed the 21st Century Cures Act authorizing \$1.8 B in funding for the Cancer Moonshot, to broadly support cancer research, and changed the name to the Beau Biden Cancer Moonshot; \$300 M are allocated for FY 2017. The FOAs have been developed to align the

recommendations with the overall goals of the Beau Biden Cancer Moonshot and overarching cross-cutting themes of health disparities, prevention, technology development, data sharing, and partnerships. Given the timing of the funding approval, the NCI was limited in time to engage the cancer research community and solicit its input on implementation of the recommendations. The goals for FY 2017 are to establish the foundation to lay the groundwork for implementing the broader initiatives in FY 2018 and FY 2019 that were outlined in the recommendations. The NCI currently is positioned to accelerate the progress of 5 of the 10 research areas for FY 2017 and support several new initiatives. The full list can be accessed on NCI's Cancer Moonshot website: [www.cancer.gov/brp](http://www.cancer.gov/brp).

For FY 2018 and FY 2019, the NCI has designed a more structured implementation process that would allow input from both the NCI community and the broader cancer research community to accommodate the different and disparate recommendations. Twelve Cancer Moonshot Implementation Teams (CMITs) will be aligned with the 10 BRP recommendations; cancer immunology will have both adult and pediatric CMITs, and prevention and early detection will have both cancer screening and prevention CMITs. These 12 CMITs, comprising more than 250 representatives from NCI's intramural and extramural communities and other Institutes, will be charged to discuss approaches and develop initiatives for FY 2018 and FY 2019 that will achieve the goal of the recommendation. The CMITs will identify gaps and opportunities in the existing initiatives; seek input from others, including the NCAB, advocacy groups, and associations; and leverage existing partnerships. In addition, the CMITs are charged to provide oversight and coordination of the funded initiatives. To address communications across CMITs, which will be critical to the success of the implementation plan, the NCI is proposing to establish an Implementation Coordinating Committee (ICC) that would convene bimonthly meetings with coordinators who are assigned to each CMIT to share ideas and cross-cutting information and to discuss concepts. In parallel, an Implementation Partnership Committee would engage the appropriate partners for the research initiatives as they are being developed. Information on high-priority concepts would be forwarded to an Implementation Steering Committee for review and, from there, would be forwarded to NCI's Scientific Program Leaders for budgetary considerations and approval. The implementation plan is moving rapidly—the CMITs meet weekly and the ICC meets every 2 weeks—nine proposals from six different CMITs have been reviewed. Dr. Singer conveyed NCI's enthusiasm for implementing the Beau Biden Cancer Moonshot recommendations as shared by all of the NIH.

**In the discussion, the following points were made:**

- Members encouraged the NCI to develop ways to leverage the NCI-MATCH trial and the existing infrastructure to inform other precision medicine clinical trials for patients with advanced stage cancers. The opportunity exists to gain more insight into patient relapse and drug resistance by use of serial biopsies.
- The NCI Formulary provides an opportunity for NCI-designated Cancer Centers, individually or as partners, to conduct NCI-MATCH-like trials.

**IV. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI PROGRAM STAFF**

**Office of the Director and Division of Cancer Biology**

**Role of HIV Infection, Sequelae Associated with HIV Infection, or Antiretroviral Therapy, in Modulating the Tumor Niche in Cancer (New RFA)**

Dr. Elizabeth Read-Connole, Program Director, DCB, presented a new concept on the role of HIV Infection, Sequelae Associated with HIV Infection, or Antiretroviral Therapy in Modulating the Tumor Niche in Cancer. Dr. Read-Connole stated that the purpose of this RFA, which was developed in collaboration with OHAM, is to advance understanding of the risks, development, progression, biology,

diagnosis, and treatment of malignancies observed in individuals with an underlying HIV infection. She noted that this research was prioritized by the OAR, NIH, as high-priority AIDS research and will investigate the role of the tumor niche (e.g., microenvironment) in HIV-related cancer. The concept aligns with the OAR FY 2017 Strategic Plan and thus will provide answers to major scientific questions. Members were also informed that applications will be accepted in two cycles with two award dates and will be reviewed by a special review panel composed of subject-matter experts convened by the NCI Division of Extramural Activities.

**Subcommittee Review.** Dr. Daniel C. DiMaio, Waldemar Von Zedtwitz Professor and Vice Chairman of Genetics, Department of Genetics, Professor of Therapeutic Radiology and Molecular Biophysics and Biochemistry, Deputy Director, Yale Cancer Center, Yale University School of Medicine, expressed the Subcommittee's support for the concept. Dr. DiMaio noted that lung cancer and other common forms of cancer are the leading cause of death in persons infected with HIV. As such, the microenvironment will be important in understanding these HIV-related cancers. He stated that the Subcommittee expressed concern with the proposal for a Special Emphasis Panel to review the applications, which could be reviewed in the regular Center for Scientific Review Study Sections.

**In the discussion, the following points were made:**

- Members encouraged the NCI to engage experts of the appropriate scientific disciplines who are serving on the Center for Scientific Review's standing Study Sections when establishing the NCI Special Emphasis Review Panel.

The first year's cost for the one-time issuance is estimated at \$2 M for four to five R01 awards, with a total cost of \$20 M for 5 years.

**Motion.** A motion to concur on the Office of the Director and DCB's RFA concept entitled "Role of HIV Infection, Sequelae Associated with HIV Infection, or Antiretroviral Therapy in Modulating the Tumor Niche in Cancer" was amended to include members with the appropriate scientific expertise serving on the Center for Scientific Review's standing Study Sections on the NCI Special Emphasis Review Panel. The was approved unanimously.

## **Division of Cancer Prevention**

### **Consortium on Translational Research in Early Detection of Liver Cancer (New RFA/Coop. Agr.)**

Dr. JoAnn S. Rinaudo, Program Director, DCP, presented a new concept to establish a consortium on translational research in the early detection of liver cancer. Dr. Rinaudo stated that the purpose of the RFA is to establish a liver cancer consortium that will improve the surveillance of hepatocellular carcinoma (HCC) in high-risk populations, increase the percentage of HCC detected at an early stage, and better stratify high-risk patients for effective treatments. In the United States, the hepatitis C virus accounts for 50 to 60 percent of HCC cases and hepatitis B virus accounts for 20 percent. Nonviral etiologies or risk factors include obesity, which can lead to nonalcoholic fatty liver disease and nonalcoholic steatohepatitis (NASH), representing 4 to 13 percent of HCC cases; alcoholic liver disease accounts for 4 percent. Dr. Rinaudo noted that this concept aligns with recent recommendations from the U.S. Senate Committee on Appropriations, a 2014 NCI workshop, DHHS, and the American Association for the Study of Liver Disease to support research on HCC surveillance and early detection.

Members were told that the research objectives for establishing a Translational Liver Cancer Consortium (TLC) are to identify and establish cohorts of patients at high risk for liver cancer; stratify cirrhosis patients into high-risk groups; identify biomarkers of HCC; and identify changes in the viral genome. The NCI will leverage resources of other consortia, including the NCI HCC Epidemiology Consortium, the

National Institute of Diabetes and Digestive and Kidney Diseases' NASH Clinical Research Network, and the National Institute on Alcohol Abuse and Alcoholism's Translational Research and Evolving Alcoholic Hepatitis Treatment.

**Subcommittee Review.** 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 Langone Medical Center, New York University School of Medicine, indicated the Subcommittee's enthusiasm and support for the concept. Dr. Bar-Sagi stated that the Subcommittee appreciates NCI staff responses to their questions about the scope of the project, integration of new biomarkers, leveraging existing NCI and NIH programs, and evaluation criteria for success.

**In the discussion, the following points were made:**

- The RFA should include more clarity on the research objective to establish cohorts of patients at high risk for liver cancer for the TLC. The expectations are that the consortium would strategically extend its research efforts past establishment and identification.
- The acceptance criteria should include details to establish cohorts that are representative of the diverse populations in the United States. Existing cohorts from other Federal agencies—such as the Federal Bureau of Prisons and the U.S. Department of Veterans Affairs—should be leveraged.
- The proposed funding may be inadequate to support the goals of the proposal to establish new cohorts of patients at high risk for HCC.

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

**Motion.** A motion to concur on DCP's RFA/Coop. Agr entitled "Consortium on Translational Research in Early Detection of Liver Cancer" was approved unanimously.

#### **V. ONGOING AND NEW BUSINESS—DR. CHI V. DANG**

Dr. Dang thanked members and presenters for their participation and comments. Members were reminded to send potential agenda topics for future Board meetings to Dr. Gray.

#### **VI. ADJOURNMENT—DR. CHI V. DANG**

There being no further business, the 58<sup>th</sup> regular meeting of the BSA was adjourned at 2:42 p.m. on Tuesday, 21 March 2017.

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Date

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Chi V. Dang, M.D.  
Chair, Board of Scientific Advisors

\_\_\_\_\_  
Date

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