With the submission of the NRG Oncology grant proposal to the National Cancer Institute (NCI) on January 15, the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG) took the formal step toward becoming the cancer clinical cooperative group NRG Oncology. These three groups have more than 150 years’ cumulative experience in conducting practice-defining, multi-institutional phase II and III trials sponsored primarily by the NCI, as well as a history of undertaking the kind of phase I trials and translational biological studies that will be imperative for future clinical cancer research.

The three legacy groups will continue to carry out NCI-supported trials as independent but collaborative entities through February 2014, with 96 total trials open for patient accrual and 68 trials in development. If all goes as planned, beginning in March 2014, NRG Oncology’s federal research activities will be managed under the auspices of the NRG Oncology Operations Center. The three current chairs, Walter J. Curran, MD; Philip J. DiSaia, MD; and Norman Wolmark, MD, will serve as NRG Oncology principal investigators (PIs) and share equal responsibility for executing the group’s research program.

**Legacy Groups’ Histories Provide Strong Foundation**

The NSABP, RTOG, and GOG each bring strong scientific credentials and a solid history of contribution to the cancer research effort.

The NSABP’s trials have had a profound impact on the treatment of breast and bowel cancer and our understanding of the biology of these diseases. The group is perhaps best known for its series of surgical breast cancer studies that led to the elimination of the radical mastectomy and the confirmation that lumpectomy plus radiation therapy (RT) is an effective option for most women with invasive or noninvasive breast cancer. The group also conducted a series of adjuvant therapy trials that evaluated systemic treatments for patients with node-positive, node-negative, and ductal carcinoma in situ (DCis) breast cancer and a series of adjuvant therapy trials for patients with colon and/or rectal cancer. Many of today’s standard adjuvant therapy regimens result directly from these trials. NSABP research was central to the development of the Oncotype Dx® tool for assessing recurrence risk and predictive significance of chemotherapy in women with early-stage, hormone receptor-positive cancer. Neoadjuvant therapy for the treatment of operable breast cancer, a current research focus of the group, is an approach that allows for high breast preservation and tumor downstaging rates and provides serial tumor specimen collections for early response assessment. The NSABP Biorepository houses tissue blocks, serum, and lymphocytes from more than 70,000 patients entered into NSABP breast and colorectal cancer trials and represents a valuable resource for current and future correlative science efforts for these diseases.

RTOG research has set and/or validated many of the national and international standards for combined modality therapy of localized to intermediate-stage cancer in adult brain tumors, head and neck cancer, localized or locally advanced lung cancer, noncolorectal gastrointestinal cancer, genitourinary cancer, and localized and locally advanced prostate cancer. A number of recent RTOG-led trials have defined new practice standards: the first randomized brain tumor trial defining chromosomal deletions as prognostic and predictive biomarkers; the first phase III trial defining concurrent chemoradiation as the standard of care for laryngeal preservation; the phase III trial helping to decrease overtreatment by demonstrating the lack of survival benefit for routine inclusion of surgery in management of patients with mediastinal lymph node-positive non-small-cell lung cancer (NSCLC); and a series of trials clarifying the role and optimal duration of total androgen blockade for men with localized, locally advanced, or locally recurrent prostate cancer.

GOG embodies the only significant effort in the current cooperative group system to study gynecologic cancers and is regarded internationally as the leader in clinical trials in this domain. GOG research has yielded many practice-defining advances in the management of gynecologic cancers: 1) defining the current international standard of care for women with advanced ovarian cancer; 2) establishing intraperitoneal chemotherapy as the treatment of choice in the management of small-volume-residual advanced ovarian cancer; 3) identifying concurrent cisplatin-based chemoradiation as the treatment of choice for stages IB2-IVA carcinoma of the uterine cervix; 4) evolving the current treatment of choice for advanced or recurrent carcinoma of the cervix; 5) defining the spread pattern of endometrial carcinoma, currently the most common gynecologic cancer, which established the basis for the therapeutic evolution in early-stage endometrial carcinoma; 6) changing the paradigm for the management of locally
advanced endometrial carcinoma by demonstrating roles for systemic therapy; 7) developing effective combination chemotherapy for advanced or recurrent endometrial carcinoma; and 8) setting the current standard of care for patients with uterine sarcomas, thought to be too uncommon to permit large trials, through a series of phase III studies.

NRG Oncology, by combining the resources and creative scientific energy of the three strong legacy groups, will create a synergy capable of a far-reaching impact.

**NRG Oncology Scientific Focus**

Internationally recognized investigators populate the leadership and membership of all seven cancer disease site committees encompassed by NRG Oncology. In addition, as the result of the history of its legacy groups, NRG Oncology will bring extensive experience in the conduct of trials not only in the United States but also overseas and in Canada; every NCI-designated cancer center in the United States that conducts clinical research and every lead provincial cancer center in Canada participates in one or more of NRG Oncology’s three legacy groups.

NRG Oncology will focus on the following diseases:

- Adult brain tumors (primary and secondary)
- Head and neck cancer
- Localized and locally advanced lung cancer (both NSCLC and small-cell lung cancer [SCLC])
- Breast cancer
- Gastrointestinal cancer (including colorectal and noncolorectal)
- Genitourinary cancer (emphasizing nonmetastatic prostate and bladder)
- Gynecologic cancer (including ovarian, cervix, and endometrial)

We anticipate that the emphasis on these seven disease sites will complement the research missions and clinical trial portfolios of the other groups within the National Cancer Trials Network (NCTN), particularly given NRG Oncology’s unique multidisciplinary strengths in gender-specific cancers, aerodigestive malignancies, and brain tumors. In addition, the group’s mission will focus on patients with localized and intermediate-stage malignancies, an emphasis that is relevant to all seven of NRG Oncology’s cancer disease sites.

NRG Oncology will be uniquely positioned in four specific arenas. The three legacy groups all have a history of practice-defining trials of new multidisciplinary approaches to localized or locally advanced cancer. The new group’s mission to improve the lives of cancer patients with these forms of disease through the conduct of high-quality clinical trials is ideally suited to the multimodality research that the new group will conduct.

NRG Oncology will also be especially positioned with regard to the study of clinical trials in breast, gynecologic, and prostate cancers. NRG Oncology’s new configuration will offer new opportunities to examine common pathways of hormonal resistance across these diseases, to develop interactive strategies to overcome hormonal resistance, to study populations at high risk for late disease failure, and to study populations at special risk of developing hormone-responsive malignancies. There are also opportunities to study outcomes beyond survival and disease-free survival (DFS), including sexual functioning and other patient-reported outcomes, as well as comparative-effectiveness research.

In addition, NRG Oncology will be capable of developing and testing innovative advanced radiation oncology technology across the NCTN through its Center for Innovation in Radiation Oncology. This center’s capabilities will allow the group to expand the transformational work conducted in its legacy groups to systematically evaluate new methods of planning and delivering therapeutic radiation; specifically, NRG Oncology will be positioned to design and execute trials that evaluate new radiation oncology approaches to cancer treatment.

Finally, as a result of the landmark translational science results from the group’s legacy committees, the new group’s combined efficiencies should result in trials that are at the forefront of such work. NRG Oncology’s trials will emphasize the use of biomarkers to stratify patients with potentially curable malignancies to therapeutic regimens that are designed to truly reflect both the risk of tumor recurrence and the risk of therapy-related toxicities. Efforts currently under way to better understand the biological underpinnings of patient-reported toxicities and to evaluate pathways and mechanisms for interventions will be enhanced once the three legacy groups are united. NRG Oncology’s translational science program will have a strong foundation in tumor and tissue procurement, processing, and storage procedures in conjunction with its biorepository sites in Pittsburgh, San Francisco, and Columbus. Collectively, these laboratories contain more than 797,400 annotated specimens.

Other goals for NRG Oncology include research into rare tumors, mentoring new investigators, expanding NRG Oncology membership, improving the enrollment of underserved populations in the group’s trials, and offering resources for non-NCTN investigator-initiated trials.
Organizational Structure

The figure below illustrates the new entity’s organizational structure. The group’s functional organization is the NRG Oncology Foundation, Inc., a 501(c)(3) entity formed in 2012 within the Commonwealth of Pennsylvania and the organization to which all governmental grants that support the NRG Oncology portfolio will be awarded.

In addition to the three chairs, six NRG Oncology deputy group chairs will lead specific group functions:

- Research Strategy: Mitchell Machtay, MD
- Protocol Prioritization and Conduct: J. Tate Thigpen, MD
- Scientific Publications: Deborah Bruner, PhD
- Membership: D. Lawrence Wickerham, MD
- Research Integrity: Larry J. Copeland, MD
- Communications: Michael J. O’Connell, MD

NRG Oncology Foundation, Inc. Board of Directors.

This board will be chaired by one of NRG Oncology’s group chairs and will consist of 17 members: the three group chairs, six appointments by the chairs, three representatives from the institutions, the contact PI for the NRG Oncology Statistical and Data Management Center (SDMC), a patient advocate, an outside financial expert, a Community Clinical Oncology Program (CCOP) representative, and an ad hoc member appointed by the group chairs. The board will ensure the appropriate allocation of NRG Oncology resources, allowing the group to fulfill its mission of improving the lives of adults with localized or locally advanced malignancies through the conduct of multi-institutional research trials. All other committees will be responsible for submitting or presenting their reports and recommendations to the board for review.

External Scientific Advisory Board (ESAB). This group will consist of investigators experienced in the conduct of high-quality clinical and translational research to assess the group’s success in fulfilling its mission. They will not be current NRG Oncology members. The ESAB will meet at least annually to review the group’s progress. Members of the ESAB will be appointed by the group chairs and will report recommendations to them.
Overview of Committees
The Concept Prioritization Advisory Committee, Research Strategy Committee, various scientific committees, and administrative committees, as shown in the figure below, will carry out research planning and the implementation of NRG Oncology functions.

NRG Oncology Group Executive Committee
This committee will comprise the NRG Oncology group chairs, the deputy group chairs, the group statisticians, and the executive directors of the Operations Center, and will be chaired by the presiding group chair. It will meet regularly to ensure that the priorities set by the Foundation board are operationalized in the group’s research strategy and supported by appropriate Operations Center resources. This committee will be advisory to the group chairs and not a decision-making committee.

Disease Site Committees
The seven cancer disease site committees (brain tumor, head and neck cancer, lung cancer, breast cancer, gastrointestinal cancer, genitourinary cancer, and gynecologic cancer) will be the units within which most protocols will be developed and executed. The group chairs will appoint the leaders of these committees for 5-year terms, and for no more than two successive terms per individual. Chairs of these committees also will participate in the NCI disease site steering committees, each of which will be responsible for developing both long- and short-term strategic research plans for common and rare malignancies in their domain and for presenting these visions to NRG Oncology’s Research Strategy Committee.

Non-Disease Site Scientific Committees
In addition to the disease site committees, four other committees will conduct NRG Oncology trials as well as support research within the disease site committees: the Translational Science (TS), Developmental Therapeutics (DT), Cancer Prevention and Control (CPC), and Patient-Centered Outcomes Research (PCOR) committees.

Scientific Core Committees
Seven scientific core committees will serve as shared resources of expertise and, in some cases, technology, enabling disease site and non-disease site scientific committee investigators to develop and execute high-quality research trials. The leaders and co-leaders of these committees will be appointed by the group chairs and will have membership chosen for expertise applicable to the overall priorities of NRG Oncology, as well as to each of its disease site committees. They include the Pathology Committee, Surgical Oncology Committee, Medical Oncology Committee, Radiation Oncology Committee, Patient Advocate Committee, Special Populations Committee, and Protocol Support Committee.
Research Strategy Committee
This scientific committee, led by the deputy group chair for research strategy, will be responsible for coordinating the scientific agenda for the group in accordance with its strategic themes, the group’s strengths, and the research needs of the overall NCTN. The RSC will focus on study development and will provide feedback and recommendations to the disease site and scientific core committees. This committee also will provide regular reports to the NRG Oncology Foundation board.

Concept Prioritization Advisory Committee (CPAC)
Chaired by the deputy group chair for protocol prioritization and conduct, this scientific committee will provide a rigorous and objective evaluation of the scientific merit and feasibility of NRG Oncology research concepts that have been vetted by the RSC, with final recommendations, including prioritization scores, sent to the group chairs for final approval. In addition, CPAC will be responsible for monitoring the progress of active studies, for the timeliness of results reporting in concert with the appropriate scientific committee, and for reporting these activities to the NRG Oncology Foundation board.

Publications Committee
Chaired by the deputy group chair for scientific publications, this body will develop and enforce the NRG Oncology publications policy, which governs issues including manuscript development and writing, authorship, peer review, timeliness monitoring, confidentiality matters, and other issues as required. This committee will review and facilitate proposed changes to policy or to general group publications operations procedures.

Membership Committee
Chaired by the deputy group chair for membership, this committee will be responsible for establishing the criteria for initial and ongoing institutional membership for submission to and final approval by the group chairs. This committee will also review and recommend new institutions for membership in NRG Oncology and recommend corrective actions as needed for existing members.

Communications Committee
Chaired by the deputy group chair for communications, this committee will be charged with developing an effective communications strategy for its members, the oncology community, and the general public. The committee will also be responsible for developing and updating an Internet strategy for the group.

Audit/Quality Control Committee
Chaired by the deputy group chair for research integrity, this committee will oversee the NCI-mandated on-site audit program, supervise the documentation of the accuracy of the data submitted to NRG Oncology, and verify investigator compliance with regulatory and group requirements for clinical trials. The deputy group chair for research integrity will serve as the NRG Oncology research misconduct officer.

Data Monitoring Committee
Governed by the NCI Data Monitoring Policy, the DMC will review the efficacy and morbidity data for each NRG Oncology clinical trial to ensure that decisions regarding continuation of these trials are both scientifically sound and ethically responsible. The DMC will make recommendations to the group chairs for a final decision. The DMC will be chaired by a non-NRG Oncology member with appropriate qualifications for this role.