

# **NSABP Foundation, Inc.**

## **Research Development Report**

### **Reporting Period:**

July 1, 2009 - June 30, 2010

### **Commercial Development of Research**

Efforts towards the commercialization of discoveries resulting from Health Research Formula funding have resulted in the submission of four provisional patent applications related to the identification and use of predictive markers for improving cancer patient care. Under confidential agreements, the NSABP conducts an ongoing exchange of ideas with current and potential commercial partners. Documented intellectual property (IP) policies provide for NSABP ownership and the sharing of IP revenues with employees and member institutions of the Foundation. The use of biospecimens is governed by the policies of the Foundation, which, we believe, are in accordance with federal requirements. Discussions with, and final review by, scientific legal counsel specializing in intellectual property at a national law firm have resulted in contractual arrangements with commercial corporations.

The NSABP also continues to develop business relationships and opportunities in a variety of ways, including: networking at scientific meetings with companies and individuals who have novel scientific ideas and interests common to NSABP; publication of results from projects supported by Health Research Formula funding; and through NSABP's participation in business and scientific organizations, such as the Association of University Technology Managers (AUTM), Licensing Executives Society (LES), Society of Research Administrators (SRA), Oncology Nursing Society, National Histological Society, Council of Science Editors, and the American Association for Cancer Research.

The NSABP Foundation has continued to meet with the major multi-national pharmaceutical and biotechnology companies offering oncology products and serving as potential sources for commercialization. We have established contractual relationships with many of these companies to perform Phase II and III clinical trials and have signed contractual agreements providing opportunities for licensing partnerships.

### **Research Licensing Agreements**

The NSABP Foundation's license agreement template, which has been provided in previous Supplemental Information Report submissions, is used as the basis of our negotiations with potential partners. The template undergoes periodic review by legal counsel to ensure continued compliance with all laws and regulations.

## **Training Students and Health Professionals**

The Foundation recruits visiting, post-doctoral research fellows, each engaged in State-funded projects during their tenure of one or more years. The fellows use their expertise in Medicine and Anatomic Pathology to perform complete microscopic and molecular analyses of breast and colon tumors based on NSABP clinical trial protocols; develop new prognostic and predictive tests for breast cancer; and conduct research using various techniques including immunohistochemistry, fluorescence in-situ hybridization (FISH) and gene expression profiling using microarray. We have one fellow working in the pathology laboratory during the current reporting period.

The NSABP encourages the laboratory scientists to participate in external educational symposiums to allow for an ongoing exchange of scientific information with oncology colleagues.

In addition to the standard laboratory training, research fellows and laboratory staff continue to participate in on-site training in the operation of sophisticated laboratory equipment used for a variety of genetic research applications.

## **Commercial Research Development Training**

Active participation of laboratory staff and research fellows continues to be critical to scientific and development discussions where the design and examination of scientific data is discussed and finalized with potential business partners.

Senior faculty conference and consult with legal and scientific counsel regarding inventions, intellectual property, licensing agreements, and potential patent opportunities.

## **Outreach to Businesses Regarding Recent Research Developments**

NSABP employs a wide range of methods to disseminate its research findings, including publications in peer-reviewed journals, presentations, posters, and abstracts at national and international meetings. These outreach efforts are an effective means of informing both the scientific community and businesses about NSABP research developments, and will be employed to communicate research findings that may result from research funded by the health research formula fund. NSABP presentations and publications that have occurred during the reporting period are described in the following paragraphs.

NSABP continues to present its research findings in peer-reviewed journals and at national and international meetings attended by colleagues, collaborators and business partners. A partial list of the conferences where this year's presentations were made included: American Association for Cancer Research Meeting, Washington, DC; AGH Breast Conference: Genetics; Pittsburgh, PA; Current Trends in Breast Cancer, Dallas, TX and Minneapolis, MN; Global Breast Cancer Symposium: Prediction of Response to Systemic Therapy in Breast Cancer, Seoul, Korea; International Federation for Head and Neck Cancer Symposium 2010, Seoul, Korea; Korean Breast Cancer Symposium, Seoul, Korea; New Developments in Breast Cancer, Dallas, TX and

Richmond, VA; NIH Pharmacogenetics Research Network Center for Genomic Medicine, RIKEN Strategic Alliance Hawaii Meeting; NSABP Group Meetings, North American Menopausal Society (NAMS), San Diego, CA; the 27<sup>th</sup> Annual Breast Imaging Seminar, Pittsburgh, PA; Breast Cancer Update Clinical Investigator Think Tank, Miami, FL; NIH State-of-the-Science Conference, “Diagnosis and Management of DCIS”, Bethesda, MD; PA Breast Cancer Coalition, Harrisburg, PA; and the Woman’s Hospital of Texas, Houston, TX.

NSABP scientists continue to author and publish oncology articles in well-respected peer-reviewed journals. A complete list of these journals include: American Journal of Surgical Pathology; Annals of Oncology; Annals of Surgical Oncology; BioMed Central Cancer (online journal); Breast Cancer Research Treatment; Cancer; Cancer Prevention Research; Clinical Genetics; Journal of Cancer Survivorship; Journal of Clinical Oncology; Journal of the National Cancer Institute; Journal of Women’s Health (Larchmont); Nature Reviews Clinical Oncology; New England Journal of Medicine; Oncology; and Statistics in Medicine.

NSABP publications and abstracts published within this reporting period include the following:

Initial safety report of NSABP C-08: A randomized phase III study of modified FOLFOX6 with or without bevacizumab for the adjuvant treatment of patients with stage II or III colon cancer. *J Clin Oncol* 2009; 27:3385-3390.

Estimating breast cancer-specific and other-cause mortality in clinical trial and population-based cancer registry cohorts. Accepted, April, *Cancer*. *Cancer* 2009; 115:5272-5283.

Cancer survivorship research: The challenge of recruiting adult long-term cancer survivors from a Cooperative Clinical Trials Group. *J Cancer Surviv* 2009; 3(3):137-147.

Menstrual cycle and surgical treatment of breast cancer: Findings from the NCCTG N9431 study. *J Clin Oncol* 2009; 27:3620-3626.

If sentinel node micrometastases are the question, are clinical trials the answer? *J Clin Oncol* 2009; 27:4640-4641.

Surgeon training, protocol compliance, and technical outcomes from breast cancer sentinel lymph node randomized trial. *J Natl Cancer Inst* 2009; 101:1356-1362.

Case report: De novo BRCA2 gene mutation in a 35-year-old woman with breast cancer. *Clin Genet* 2009; 76:427-430.

Evaluation of microtubule-associated protein tau expression as a prognostic and predictive marker in the NSABP B-28 randomized clinical trial. *J Clin Oncol* 2009; 27:4287-4292.

Preoperative multimodality therapy improves disease-free survival in patients with carcinoma of the rectum: NSABP R-03. *J Clin Oncol* 2009; 27:5124-5130.

Use of archived specimens in evaluation of prognostic and predictive markers. *J Natl Cancer Inst* 2009; 101:1446-1452.

A new generalization of Weibull distribution with application to a breast cancer data set. *Stat Med* 2009; 28:2077-2094.

Metastasis detection in sentinel lymph nodes: Comparison of a limited widely spaced and comprehensive narrowly spaced paraffin block sectioning strategy. *Am J Surg Pathol* 2009; 33:1583-1589.

Alternating systemic and hepatic artery infusion therapy for resected liver metastases from colorectal cancer: A North Central Cancer Treatment Group (NCCTG)/ National Surgical Adjuvant Breast and Bowel Project (NSABP) Phase II Intergroup trial, N9945/ CI-66. *J Clin Oncol* 2010; 28:853-858.

National Institute of Health state-of-the-science conference statement: Diagnosis and management of ductal carcinoma in situ. September 22-24, 2009. *J Natl Cancer Instit* 2010; 102:161-169.

Efficacy and cardiac safety of adjuvant trastuzumab-based chemotherapy regimens for HER2-positive early breast cancer. *Ann Oncol* 2010 Mar 29. [Epub ahead of print]

Association between disease-free survival and overall survival when survival is prolonged after recurrence in patients receiving cytotoxic adjuvant therapy for colon cancer: Simulations based on the 20,800 patient ACCENT data set. *J Clin Oncol* 2010; 28:460-465.

Relative effects of tamoxifen, raloxifene, and conjugated equine estrogens on cognition. *J Womens Health (Larchmont)* 2010; 19(3):371-379.

A rapid, sensitive, reproducible and cost-effective method for mutation profiling of colon cancer and metastatic lymph nodes. *BMC Cancer (online journal)* 2010; 10: 101.

Identification of accrual barriers onto breast cancer prevention clinical trials: A case-control study. *Cancer* 2010 May 5. Epub ahead of print.

Population-based survival-cure analysis of ER-negative breast cancer (B-22, B-25, B-28). *Breast Cancer Res Treat* 2010; Feb 4. Epub ahead of print.

Gene expression-based prognostic assays for breast cancer. *Nat Rev Clin Oncol* 2010; 7:340-347.

Association between the 21-Gene Recurrence Score Assay and risk of locoregional recurrence in node-negative, estrogen receptor-positive breast cancer: Results from NSABP B-14 and NSABP B-20. *J Clin Oncol* 2010; 28:1677-1683.

Targeting alternative pathways in HER2-positive breast cancer. *Oncology* 2010; 24:415-416.

Definitive analysis of patient outcomes from a randomized phase III trial evaluating three different schedules and combinations of adjuvant therapy containing doxorubicin, docetaxel, and

cyclophosphamide in women with operable, node-positive breast cancer: Results of the NSABP B-30 trial. *New Engl J Med* 2010; 362:2053-2065.

Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. *Cancer Prev Res* 2010; 3:696-706.

Long-term survival results of surgery alone versus surgery plus 5-fluorouracil and leucovorin for stage II and stage III colon cancer: Pooled analysis of NSABP C-01 through C-05. A baseline from which to compare modern adjuvant trials. *Ann Surg Oncol* 2010; 17:959-966.

Conditional survival and the choice of conditioning set for patients with colon cancer: An analysis of NSABP trials C-03 through C-07. *J Clin Oncol* 2010; 28:2544-2548.

Kuerer H, Ed. Book. *Kuerer's Breast Surgical Oncology*. NY, McGraw-Hill. Published, Feb 2010.

NSABP scientists have also presented study results from NSABP clinical trials in the form of abstracts and posters. The following list summarizes those presentations:

National Institute of Health Consensus Conference on DCIS:

NSABP B-39, B-43 – Sentinel lymph node biopsy and management of the axilla. Presented.

NSABP B-35 – Quality of life issues and outcomes research in DCIS. Presented.

NSABP B-24 – Presented.

National Society of Genetic Counselors:

De novo BRCA2 gene mutations: A case report and review of the literature. National Society of Genetic Counselors, Atlanta, GA. Abstr 607. Poster presentation. Presented.

American Association for Cancer Research (AACR), Molecular Targets and Cancer Therapeutics :

NSABP C-07 – Mutation profiling and prognostic value of BRAF, HRAS, KRAS, MET, NRAS, PIK3CA, KRASG12V in colon cancer: Results from NSABP C-07. Abstr A201.

American Association for Cancer Research, Frontiers in Cancer Prevention Research Conference:

Cancer prevention clinical trials: Assessing for disparities in recruitment in Hawaii. Presented.

San Antonio Breast Cancer Symposium:

NSABP B-32 – Predictive factors for positive non-sentinel nodes following a positive sentinel node biopsy. Poster discussion. Abstr 301.

American Association of Clinical Radiology:

Update of the NSABP Study of tamoxifen and raloxifene (STAR) P-2 trial in preventing breast cancer. Presented.

American Society of Clinical Oncology (ASCO):

Outcomes following adjuvant treatment (AT) for colon cancer (CC) 1978-1995 vs 1996-2007: impact on recurrence rate, time from recurrence to death (TRD) and overall survival (OS); Findings from the ACCENT dataset. Poster. Abstr 3616. J Clin Oncol/ASCO 2010.

Time-dependent patterns of treatment effect and failure help explain the predictive role of deficient mismatch repair (dMMR) in stage II and III colon cancer (CC). Poster discussion. Abstr 3518. J Clin Oncol/ASCO 2010.

Primary outcome results of NSABP B-32, a randomized phase III clinical trial to compare sentinel node resection (SNR) to conventional axillary dissection (AD) in clinically node-negative breast cancer patients. Selected as a “Best of ASCO” abstract. LBA 505. J Clin Oncol/ASCO 2010.

Quality of life and symptoms in long-term survivors of colorectal cancer: Results from NSABP Protocol LTS-01. Poster discussion. Abstr 9035. J Clin Oncol/ASCO 2010.

Cigarette smoking, fitness, and obesity as predictors of chemoprevention adherence among women in the National Surgical Adjuvant Breast and Bowel Project (NSABP) Breast Cancer Prevention Trial (BCPT). Poster discussion. Abstr 1524. J Clin Oncol/ASCO 2010.

A phase II trial of 5-fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6) chemotherapy plus bevacizumab for patients with unresectable stage IV colon cancer and a synchronous asymptomatic primary tumor: Results of NSABP C-10. Poster discussion. Abstr 3527. J Clin Oncol/ASCO 2010.

Comparison of molecular and pathologic features of stage II and stage III colon cancer in 4 large studies conducted for development of the 12-gene colon cancer recurrence score. Oral presentation. Abstr 3503. J Clin Oncol/ASCO 2010.

Combination of prognostic gene index + nodal status identifies subset of stage II/III colon cancer patients who may not need oxaliplatin-containing adjuvant chemo. Poster presentation. Abstr 3516. J Clin Oncol/ASCO 2010.

Benefits and adverse events in younger (age <50) vs older patients receiving adjuvant chemotherapy for colon cancer: Findings from the 33,574 pt ACCENT dataset. Poster discussion. Abstr 3523. J Clin Oncol/ASCO 2010.

DNA mismatch repair status and site of tumor recurrence in stage II and III colon cancers treated in 5-fluorouracil-based adjuvant therapy trials. Poster discussion session. Abstr 3519. J Clin Oncol/ASCO 2010.

Recurrence risk of node-negative and ER-positive early-stage breast cancer patients by combining recurrence score, pathologic, and clinical information: A meta-analysis approach. Oral presentation. Abstr 509. J Clin Oncol/ASCO 2010.

American Society of Clinical Oncology – Gastro-Intestinal (ASCO GI):

Comparison of molecular and pathologic features of stage II and stage III colon cancer in 4 large studies conducted for development of the 12-gene colon cancer recurrence score. ASCO GI Cancers Symposium 2010. Abstr ASCO GI 280.

5-FU and leucovorin (Lv) with or without oxaliplatin (Ox) for adjuvant treatment of stage II and III colon cancer: long term follow-up of NSABP C-07 with survival analysis. ASCO GI Cancers Symposium 2010. Abstr ASCO GI 401.

Society of Surgical Oncology (SSO):

Number of nodes examined and the 12 Gene Colon Cancer Recurrence Score predict recurrence in stage II colon cancer in 2 independent studies. SSO 2010; 17(Suppl 1):S85. Abstr P162.

Individual item analysis of quality of life assessments related to laparoscopic-assisted colectomy in the COST trial 93-46-53 (INT 0146). SSO 2010; 17(Suppl 1):S36. Abstr 93.

Continuing education seminars, in collaboration with pharmaceutical partners, have recently been presented by NSABP physicians. A partial list of these seminars includes: “Breast Cancer in Perimenopausal Women”; “Advances in HER2-Targeted Therapies for Early-Stage and Metastatic Breast Cancer” “Interpreting Clinical Trial Results for Adjuvant Hormonal Therapy for Breast Cancer, “Challenging Cases in Early Breast Cancer”, “Estimated Risk of Invasive Breast Cancer in Caucasian Postmenopausal Women with Osteoporosis Using the Gail Model Compared with US General Population”, “Update on Primary Cancer Prevention”, “NSABP History and Contributions to the Treatment of Breast and Colorectal Cancers”, and “The High Risk Patient. What Does This Mean?”

**Research Development Collaboration**

The NSABP Foundation, Inc. has been in negotiation with numerous laboratory and biotechnology multi-national and Pennsylvania firms. We have also developed collaborative projects with academic institutions where we have material transfer agreements using tumor biospecimens from the NSABP Biospecimen Bank. Results of these collaborations are not yet available.

In addition, the NSABP meets on a regular basis with pharmaceutical and biotechnology companies to review drugs and laboratory techniques currently under development, or to explore opportunities for further investigation and potential commercialization. Such meetings are held under an executed confidentiality agreement.