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**FIRST PATIENT ENROLLED IN GLOBAL PHASE III STUDY  
OF BEVACIZUMAB AND TRASTUZUMAB IN EARLY BREAST CANCER**

*Collaborative groups set out to confirm potential  
benefits of anticancer therapies to treat women with breast cancer*

**Paris, France, May 27, 2008-** A new international study for women with HER2-positive breast cancer is open for enrollment. The pivotal BETH (**BE**vacizumab and **T**rastuzumab Adjuvant Therapy in **HER2**-positive Breast Cancer) study is a Phase III clinical research trial that is investigating the benefits of combining two monoclonal antibodies, the anti-angiogenic, bevacizumab (Avastin<sup>®</sup>) and the targeted therapy trastuzumab (Herceptin<sup>®</sup>), together with chemotherapy for the treatment of patients with early stage HER2-positive breast cancer.

“Trastuzumab is already the standard of care across all stages of HER2-positive breast cancer and has a proven survival benefit. Bevacizumab has been shown to be of benefit when given in combination with chemotherapy for the treatment of metastatic breast cancer,” said Dennis Slamon, MD, director of clinical/translational research at the University of California, Los Angeles’ (UCLA) Jonsson Comprehensive Cancer Center and principal investigator, Cancer International Research Group. “The design of the BETH clinical trial is based on the preclinical and early clinical work from the Slamon/TRIO Laboratories at UCLA. We are looking forward to investigating the additional benefit to patients of combining these two treatments with chemotherapy in the treatment of early breast cancer.”

“Despite treatment advances, over 400,000 women worldwide still die from breast cancer every year, so striving to improve treatment outcomes remains critical,” said Norman Wolmark, MD, chairman of the Department of Human Oncology at the Allegheny General Hospital, and principal investigator, NSABP Foundation, Inc., Pittsburgh, Pennsylvania, USA, who welcomes the start of the study.

In BETH, patients will be randomized to a regimen of chemotherapy (either 6 cycles of docetaxel/carboplatin or 3 cycles of docetaxel, followed by 3 cycles of FEC<sup>i</sup>) plus trastuzumab with or without bevacizumab.

BETH was developed through the collaborative efforts of the NSABP (National Surgical Adjuvant Breast and Bowel Project) and CIRG (Cancer International Research Group). The study will be led by the two groups and will recruit approximately 3,500 patients. The primary outcome measure of BETH will be invasive disease-free survival. Secondary endpoints for the study include disease-free survival, overall survival, safety, and tolerability.

Bevacizumab and trastuzumab are used in the treatment of women with breast cancer; bevacizumab for metastatic breast cancer and trastuzumab for both early and late HER2-positive breast cancer. This is the first Phase III trial to evaluate combining the two therapies in treating early stage breast cancer.

#### **ABOUT THE CANCER INTERNATIONAL RESEARCH GROUP (CIRG) AND TRANSLATIONAL RESEARCH IN ONCOLOGY (TRIO)**

CIRG is a not-for-profit research organization with offices based in Paris, France and Alberta, Canada. With an international network of 2000 investigators and 450 cancer centers in over 45 different countries, CIRG has conducted a number of new and innovative global studies evaluating systemic therapy for cancer. The BCIRG 001 study led to the registration of docetaxel in the early breast cancer setting. The BCIRG 006 study showed that a non-anthracycline Herceptin-containing regimen was as efficacious as an anthracycline- and Herceptin-containing regimen in the early HER2-positive breast cancer setting, thus providing an equally effective, less cardiotoxic alternative to women with this type of breast cancer.

Recently, CIRG has partnered with the UCLA-based investigator network of Translational Oncology Research International, to form TRIO (Translational Research in Oncology). In addition to a network of dedicated investigators and clinical trial services, TRIO also includes the Slamon/TRIO laboratories at UCLA. Slamon and fellow scientists have developed and adapted preclinical models which allow for the validation of molecular markers, the preclinical assessment of new biologic agents and the characterization of an agent's mechanisms of action. This preclinical work, in turn, generates the clinical hypotheses for the group's future cancer trials in patients. This translational approach has been used in the BCIRG 006 study and the newly-launched BETH clinical trial.

TRIO is dedicated to advancing translational cancer research by bringing innovative and targeted therapeutics to clinical practice. Additional information is available on the Internet at <http://www.trioncology.org>.

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<sup>i</sup> FEC refers to 5-Fluorouracil, Epirubicin, Cyclophosphamide

## **ABOUT THE NATIONAL SURGICAL ADJUVANT BREAST AND BOWEL PROJECT (NSABP)**

Headquartered in Pittsburgh, Pennsylvania, USA, the National Surgical Adjuvant Breast and Bowel Project (NSABP) is a clinical trials cooperative group. The NSABP has over a 50-year history of designing and conducting clinical research trials that have changed the way breast cancer is treated and, more recently, prevented.

With research sites at nearly 1,000 major medical centers, university hospitals, large oncology practice groups, and health maintenance organizations in the United States, Canada, Puerto Rico, and Ireland, the NSABP has enrolled more than 110,000 women and men in clinical trials in breast and colorectal cancer. More than 5,000 physicians, nurses, and other medical professionals conduct NSABP treatment and prevention trials.

NSABP breast cancer studies led to the establishment of lumpectomy plus radiation over radical mastectomy as the standard surgical treatment for breast cancer. In addition, the NSABP was the first to demonstrate that adjuvant therapy could alter the natural history of breast cancer, thereby increasing survival rates. The group was also the first to conduct large scale breast cancer prevention studies that showed that the drugs tamoxifen and raloxifene could reduce the risk of developing invasive breast cancer by about 50 percent in women at increased risk for the disease; more than 33,000 women participated in the *Breast Cancer Prevention Trial (BCPT)* and *Study of Tamoxifen and Raloxifene (STAR)*.

Additional information about the NSABP is available on the Internet at [www.nsabp.org](http://www.nsabp.org).

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