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PRINCIPAL INVESTIGATOR: Holly Gallion, M.D.

CONTRACTING ORGANIZATION: Precision Therapeutics, Inc.
Pittsburgh, PA 15203

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14. ABSTRACT PTI has received WIRB approval and the University of Pittsburgh IRB approval for this study. PTI has engaged 19 research sites in this research and four contracts have been successfully negotiated and executed. Another six research sites are determining clinical and budgetary feasibility. Pending the approval of the DoD and the WIRB of this first set of research sites submitted for approval, it is anticipated we will have the first patient enrolled in July, 2009.					
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Table of Contents

	<u>Page</u>
Introduction.....	4
Overall Progress	4
Problem Areas.....	9
Work to be Performed in Next Quarter	9
Key Research Accomplishments.....	N/A
Reportable Outcomes.....	N/A
Conclusion	N/A
References	N/A
Supporting Data	N/A

Introduction

The objective of this study is to develop a biomarker to predict pathological complete response in women treated with neoadjuvant chemotherapy for breast cancer. Such a biomarker would assist physicians in selecting the most effective chemotherapy for the individual patient. The anticipated biomarker will take into account clinical factors (such as tumor stage, tumor size, and age), phenotypic characteristics of the tumor (determined by pathological immunohistochemistry and *ex vivo* chemoresponse assay), and genotypic characteristics of the tumor and patient (determined by genomic profiling via gene expression analysis of tumor RNA). It is expected that collective consideration of all of these factors will be more predictive of patient response to therapy than any of them alone.

Approximately 224 evaluable subjects will be recruited from approximately 1 to 15 US sites. Women with measurable operable breast cancer diagnosed by core needle biopsy will be eligible for this study. Tumor specimens will be obtained prior to the start of chemotherapy via core needle biopsies to be used in the *ex vivo* chemoresponse assay and tumor genomic analysis (gene expression), respectively.

All subjects will receive neoadjuvant chemotherapy with a regimen that must consist of the following agents: doxorubicin (A), cyclophosphamide (C), and a taxane (T) such as docetaxel, paclitaxel, or Abraxane (nanoparticle albumin-bound paclitaxel [nab-paclitaxel]). These may be administered in whatever sequence and combination the treating physician prefers.

Upon completion of chemotherapy treatment, women will undergo lumpectomy, modified radical mastectomy or other surgical procedure determined appropriate by the investigator and at that time will be evaluated for pathological response. During the patient's course of participation on the study, the treating physician will remain blinded to the results of the chemoresponse assay and genomic analysis.

If it is determined there is no pathological complete response (pCR) at the time of lumpectomy, modified radical mastectomy or other surgical procedure, PTI will make available a subsequent report to the physician containing additional information about chemotherapy drugs other than ACT that could benefit the further treatment decisions for the patient.

Overall Progress

Since the last quarterly report, PTI has worked on qualifying research sites for participation in the study, obtaining and reviewing the necessary regulatory paperwork for research sites, and negotiating contracts.

To date, there are 19 research sites interested in this protocol; all but four have fully committed to participate in the study. The four sites who are not yet committed are determining clinical and budgetary feasibility.

The Western Institutional Review Board (WIRB) approved the March 23, 2009 version of the protocol and revised consent forms on April 20, 2009, and the approval letter was forwarded to Johanna Kidwell at the DoD. The University of Pittsburgh IRB approved the protocol on June 9, 2009.

PTI anticipates the first patient on the study in July, 2009, following approval of the first research sites by the DoD.

Detailed progress made between the period of March 12, 2008 – June 12, 2009

I. April 20, 2009: WIRB approved the protocol and revised informed consent forms.

II. June 9, 2009: the University of Pittsburgh IRB approves the protocol.

III. PTI has engaged 19 study sites for participation in this research and their progress is noted below. Work has involved, querying FDA and Research Integrity websites to confirm no negative reports exist on participating investigators; working with coordinators in obtaining the regulatory documents including the site qualification survey, written policies and procedures, medical licenses and CVs, etc.; verification of human subjects training; reviewing all consent forms to ensure they comply with the protocol; negotiating clinical study contracts with administration or legal personnel representing an institution; confirming Federalwide Assurance exists and is current or reviewing/coordinating Independent Investigator Agreements (IIAs) where investigators go under the PTI FWA00009200; and finalizing the changes in the electronic data capture (EDC) system through MedNet.

An additional six sites (not included below) are considering the clinical and budgetary feasibility of this study locally.

Participating Sites	Status Update
Richard Fine, MD Advanced Breast Care 790 Church Street, Suite 410 Marietta, GA 30060	• NDA executed, PI Commitment Pending • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Susan Boolbol, MD Beth Israel Hospital 10 Union Square East, Suite 4E New York NY 10003	• NDA executed, PI indicates Commitment • Scientific Review Committee Reviewing Protocol • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Theodore Potruch, MD Breastcare 2020 Goldring Ave., Suite 206 Las Vegas, NV 89106	• NDA executed, PI indicates Commitment • Site preparing for WIRB Submission • Consent Forms Reviewed and Approved • Site Qualification Survey, Regulatory Requirements Received and Accepted • Contract Executed • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified • Pending DoD approval, site will be able to register patients

Mark Gittleman, MD Breast Care Specialists, PC 250 Cetronia Road, Suite 302 Allentown, PA 18104	• NDA executed, PI indicates Commitment • Site preparing for WIRB Submission • Consent Forms Reviewed and Approved • Site Qualification Survey, Regulatory Requirements Received and Accepted • Contract Executed • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified • Pending DoD approval, site will be able to register patients
John West, MD BreastLink 230 South Main Street, Suite 100 Orange, CA 92868	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Peter Beitsch, MD Cancer Solutions 7777 Forest Lane, Suite C-760 Dallas, TX 75320	• NDA executed, PI indicates Commitment • Site preparing for WIRB Submission • Consent Forms Reviewed and Approved • Site Qualification Survey, Regulatory Requirements Received and Accepted • Contract Executed • Federalwide Assurance Verified • Research Integrity Background Verified • Pending DoD approval, site will be able to register patients
Jason S. Cohen, MD Cedars-Sinai Medical Center 8700 Beverly Blvd. Los Angeles, CA 90048	• NDA executed, PI Commitment Pending Outcome of Scientific Review Committee Review of Protocol to Determine Feasibility • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Stephanie Akbari, MD Center for Breast Health, PC 1625 North George Mason Drive Suite 315 Arlington, VA 22205	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified

Kristine Kelley, MD DeltaMedix 236 Penn Avenue Scranton, PA 18503	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified
Shawna Willey, MD Georgetown University Hospital Lombardi Comprehensive Cancer Center 3800 Reservoir Road, NW Washington, DC 20057	• NDA executed, PI indicates Commitment • Scientific Review Committee Reviewing Protocol • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Walton Taylor, MD Leading Edge Research, P.A. 9229 LBJ Freeway Dallas, TX 75243	• NDA executed, PI indicates Commitment • Site preparing for WIRB Submission • Consent Forms Reviewed and Approved • Site Qualification Survey, Regulatory Requirements Received and Accepted • Contract Executed • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified • Pending DoD approval, site will be able to register patients
Jeffrey Falk, MD Michigan Breast Specialists 19229 Mack Avenue, Suite 38 Grosse Pointe Woods, MI 48236	• NDA executed, PI indicates Commitment • Scientific Review Committee Reviewing Protocol • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Pat Whitworth, MD Nashville Breast Center, P.C. 300 20th Avenue North, Suite 401 Nashville, TN 37203	• NDA executed, PI Commitment Pending • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified

Bernard Rimpel, MD and Mark Grand, MD Preferred Health Partners 32 Court Street, 19th Floor Brooklyn, NY 11201	• NDA executed, PI Commitment Pending Outcome of Scientific Review Committee Review of Protocol to Determine Feasibility • Site Qualification Survey, Regulatory Requirements Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
James Mackey, MD and Robin Skrean, MD Southlake Oncology 1545 E. Southlake Boulevard, Suite 280 Southlake, TX 76092	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance – will go under ours for this study • Research Integrity Background Verified
Anne Wallace, MD University of California San Diego/ Moores Cancer Center Clinical Trials Office 3855 Health Sciences Dr., MC 0698 La Jolla, CA 92093-0698	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Adam Brufsky, MD University of Pittsburgh Medical Center / University of Pittsburgh Cancer Institute / Magee Women's Hospital of UPMC 300 Halket Street Pittsburgh, PA 15213-3180	• NDA executed, PI indicates Commitment • Consent Forms Reviewed and Approved • Site Received IRB Approval • Site Qualification Survey, Regulatory Requirements Received and Accepted • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Agustin Garcia, MD University of Southern California / Norris Comprehensive Cancer Center 1441 Eastlake Avenue Los Angeles, CA 90033	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified
Ekaterina Tsiapali, MD Women and Infants Hospital of RI 101 Dudley Street Providence, RI 02905	• NDA executed, PI indicates Commitment • Site Qualification Survey, Regulatory Requirements, IRB Approval Pending • Contract Review at Site Pending • Federalwide Assurance Verified • Research Integrity Background Verified

IV. June 11, 2009, PTI is testing the electronic data capture (EDC) system for changes reflected in the current version of the study and case report forms. Addition of programming for monitoring and honoraria payments will be addressed in the next release scheduled for August, 2009.

Problem Areas

I. There have been several delays in contract negotiations at academic research centers (such as the University of Pittsburgh, University of California San Diego and University of Southern California). The process has taken more than 3 months and comments have still not been received from these research sites.

II. Some investigators and study staff have allowed their human subjects training to lapse by more than 2 years; there are delays in completing the NIH training again to obtain the necessary certificate of completion.

Work to be Performed in Next Quarter

PTI will continue to engage in site qualification, regulatory requirement processing (consent form review, IRB submissions, verification of research integrity, FWA / IIA, site survey and policy review and approval, etc.) and contract negotiation in order to open the PT-304 study at approximately 25 research sites. PTI will also obtain the letters of support from each investigator, and the approvals by both the WIRB and the DoD for each study site prior to protocol initiation at each site.

PTI is having the WIRB translate the consent forms into Spanish for several sites with Spanish-speaking patient populations.

PTI will work with MedNet to test and approve necessary changes to the database to reflect the most current version of the protocol and case report forms. PTI will determine monitoring and honoraria payment requirements and specifications to build into the system for testing and release this summer.

PTI will begin to schedule site initiation visits and train sites on both the protocol requirements and the use of MedNet's EDC system.

PTI will continue to monitor the obstacles or concerns voiced by investigators which may prevent them from participating in or accruing patients to the study.

Key Research Accomplishments

Not applicable

Reportable Outcomes

Not applicable

Conclusion

Not applicable

References

Not applicable

Supporting Data

Not applicable