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MetaStat, Inc.

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EXECUTIVE INFORMATIONAL OVERVIEW®

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MetaStat, Inc.

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Ticker (Exchange)	MTST (OTC.BB)
Recent Price (01/03/2013)	\$3.00
Shares Outstanding	~21 million
Market Capitalization	~\$63 million
Insider Ownership +>5%	37.4%
Institutional Ownership*	13.9%
EPS (Qtr. ended 08/31/2012)	(\$0.04)
Employees**	3

**Note: Institutional ownership does not include MetaStat's licensors.*

***Supporting a low-cost structure for its business, MetaStat outsources a number of its efforts and has consulting agreements with many of its researchers.*



Company Description

MetaStat, Inc. ("MetaStat" or "the Company") develops next-generation diagnostic and therapeutic products for **metastatic†** cancer—cancer that has spread from a primary tumor to other areas of the body. The Company's pipeline is based on over 15 years of research and collaboration by the Albert Einstein College of Medicine of Yeshiva University, Massachusetts Institute of Technology (MIT), Cornell University, and Italy's IFO-Regina Elena Cancer Institute. One of the core findings of this research was the discovery of a unique three-cell structure in breast tumor tissue that scientists have shown is correlated with the probability of a patient developing a metastatic tumor. Having exclusively licensed this and other technologies, MetaStat is nearing commercialization of a clinical diagnostic test called MetaSite™ *Breast*, designed to predict whether a patient's breast cancer will spread through the bloodstream to other areas of the body. The Company is also advancing two additional platforms, MenaCalc and MenaBloc, which expand its diagnostic capabilities in breast, lung, and prostate tumors as well as support the development of therapeutics for preventing or reducing tumor **metastasis**. Ultimately, MetaStat's platform technologies may improve diagnosis and treatment for up to 80% of all solid tumor cancers, including breast, prostate, lung, and bowel cancers as well as tumors in the pancreas, brain, liver, or head and neck.

Key Points

- Metastasis is the cause of up to 90% of solid tumor cancer-related deaths as it is very difficult to treat. To date, no therapies have been approved specifically to treat metastasis.
- MetaSite *Breast* has been validated in two clinical studies and is expected by the Company to have a low-cost and rapid path to market. Pending publication of results from an ongoing 500-patient study, MetaStat believes that it could begin pilot marketing the MetaSite *Breast* diagnostic test as early as the second half of 2013.
- Through license agreements with the Albert Einstein College of Medicine, MIT, Cornell, and the IFO-Regina Elena Cancer Institute, MetaStat holds rights to roughly 10 patent applications in the U.S., Canada, and Europe. Importantly, in July 2012, the Company received Notices of Allowance for two of its key patents, indicating that patent authorities have found the applications approvable.
- MetaStat's leadership is experienced in the management of public biotechnology/life sciences companies. The Company possesses a highly skilled Scientific and Clinical Advisory Board, with individuals from the Albert Einstein College of Medicine, Cornell, and MIT, who were instrumental at pioneering the academic research supporting MetaStat's product development.
- As of August 31, 2012, MetaStat's cash position was over \$1.2 million.

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Executive Overview

MetaStat, Inc. (“MetaStat” or “the Company”) is a life sciences company seeking to develop and commercialize new diagnostic and therapeutic products for **systemic** cancer metastasis—the spread of cancer from a primary tumor to other parts of the body via the bloodstream. Eighty percent of all cancers are classified as **epithelial** solid tumor cancers, including breast, lung, prostate, and colorectal cancers (four of the five largest markets), and can result in metastatic tumors.

In its development of new methods for identifying, measuring, and treating the spread of cancer, MetaStat emphasizes **personalized cancer therapies**. Personalized cancer therapy is an emerging field where physicians aim to improve the efficacy of treatment by using a tailored approach for each specific patient. MetaStat’s diagnostic tools are designed to improve the efficacy and cost burden of cancer treatment by providing physicians and patients with critical information before the course of action for treatment is finalized. Historically, many cancer therapies have been broadly prescribed to patients as part of the traditional standard of care without an understanding of how the individual’s body and tumor(s) will react. As such, many **chemotherapy** treatments are considered to be “hit or miss”—effective in some patients but highly ineffective in others. Likewise, without knowing the course that a patient’s tumor will take, some individuals may undergo unnecessary toxic and costly chemotherapy regimens or, conversely, may receive insufficient treatment, allowing the cancer to spread further.

A greater understanding of the tumor’s genetic abnormalities, as well as a profile of the patient’s immune system, could help to identify, on an individual level, more specialized therapies that offer improved efficacy and outcomes while eliminating the use of ineffective treatments that often cause significant side effects. MetaStat is working to determine, with reasonable assurance, the course that the patient’s cancer will likely take (e.g., staying local to the initial tumor site or spreading beyond the primary site as an aggressive, metastatic cancer). As a result, patients identified as high risk by MetaStat’s diagnostics can receive immediate, comprehensive treatment while low-risk patients can be spared the side effects of powerful cancer therapies, such as chemotherapy and radiation.

Over 15 years of research support MetaStat’s licensed platform technologies, which have been developed by collaborative research teams from the Albert Einstein College of Medicine of Yeshiva University, the Massachusetts Institute of Technology (MIT), Cornell University, and Italy’s IFO-Regina Elena Cancer Institute (collectively, the “Licensors”). Based on the lengthy scientific support already established for the Company’s technologies/product pipeline, as well as MetaStat’s own clinical work, the Company believes that its approaches to disease management for metastatic tumors could be applicable to approximately 80% of all epithelial solid tumor cancers, including prostate, lung, colorectal, head and neck, melanoma, and pancreatic cancers. As summarized below and detailed on pages 27-35, MetaStat’s initial focus is breast cancer, which the Company is targeting with the MetaSite™ *Breast* diagnostic test.

New technologies and tools have helped researchers gain an improved understanding of metastasis in recent years, revealing opportunities for new therapies and diagnostic tools. The Company is focused on being at the forefront of this initiative. MetaStat’s platform technologies are based on direct microscopic observation of the **mechanisms** and behaviors of metastatic cells in living, functioning human-derived tumors, which the Company believes is a competitive advantage for its product candidates.

Currently, MetaStat’s pipeline centers on three platform technologies:

- (1) MetaSite *Breast*, a near-term **prognostic** test for metastatic breast cancer risk;
- (2) the MenaCalc™ diagnostic platform, for determining risk for metastatic breast, lung, prostate, and other cancers; and
- (3) the MenaBloc™ technology, which offers potential therapeutic targets for treating metastatic disease.

MetaStat's Near-Term Product Opportunity: MetaSite *Breast*

Breast cancer is one of the most commonly diagnosed cancers for females, accounting for nearly one in three cancers afflicting U.S. women (Source: the American Cancer Society's *Breast Cancer Facts & Figures, 2011-2012*). In 2011 alone, an estimated 230,480 women were diagnosed with invasive breast cancer in the U.S., adding to the millions of women already living with a breast cancer diagnosis.

While earlier detection and improved treatments have led to lower death rates over the past two decades, breast cancer was expected to be a factor in an estimated 40,000 U.S. deaths in 2012. Currently, physicians use various prognostic factors to estimate the risk of cancer progression and spread, including tumor size, various characteristics of the tumor including grade, hormone receptor and HER2 status, and spread to lymph nodes. Physical signs and symptoms as well as family history are also considerations.

The limitation of current staging procedures is that they are indirect, and not based on cancer's mechanism. As a result, patients can be improperly classified as "high risk," subjecting them to months of aggressive chemotherapy and radiation treatments that cause a number of side effects and can dramatically impact patients' quality of life. Similarly, patients may be incorrectly classified as "low risk," preventing them from receiving timely and necessary treatment. Furthermore, as the efficacy of cancer treatment varies from person to person, the cost of the therapy and the physical and mental burdens associated with treatment may not always be justified. Studies have shown that approximately 40% of patients actually develop metastatic disease (Source: Albert Einstein College of Medicine press release, March 24, 2009).

MetaStat's Approach

MetaStat's technology focuses on predicting the risk of cancer progression based on the mechanisms involved in cancer development and metastasis. Historically, cancer cells have entered the blood vessels via unknown means. The research supporting the Company's technology has sought to identify the structural and behavioral mechanisms that allow cancer cells to move and determine how this information can be used in prognosis. To MetaStat's knowledge, its technology is the only technique to focus on such mechanistic markers. Initially, the Company anticipates that its MetaSite *Breast* test, which analyzes metastatic risk by taking mechanistic factors of metastasis into account, could be used in conjunction with existing diagnostics, including Genomic Health, Inc.'s (GHDX-NASDAQ) Oncotype DX® Breast Cancer Assay, which largely estimate metastatic risk based on cancer cell proliferation. As further data for the MetaSite *Breast* is published and the test gains awareness in the clinical community over time, MetaStat believes that its test could ultimately be used as a standalone product—potentially becoming directly competitive to existing **assays** at a lower cost than currently available products.

The cornerstone of MetaStat's technology was the discovery of a three-cell structure, composed of a **macrophage**, a carcinoma cell, and an endothelial cell (collectively termed a "MetaSite"), that is believed to play a crucial role in allowing metastatic cells to enter into the bloodstream and spread through the blood to other organs in the body. The presence and function of the MetaSite was identified by a collaboration of scientists from MIT, the Albert Einstein College of Medicine, and Weill Cornell Medical College, who reasoned that the quantity of MetaSites was correlated to the probability of distant tumor metastases.

Subsequently, the team of researchers developed the MetaSite *Breast* test, a clinical laboratory assay to predict the likelihood of an early-stage breast cancer patient's tumor spreading to distant body parts. MetaSite *Breast* employs conventional **immunostaining** techniques to highlight these unique three-cell structures in tumor tissue **samples** for pathologists to clearly see and count. Each patient sample is given a Metastasis Score based on the number of MetaSites as well as an accompanying interpretation of what the score indicates in terms of the risk of developing metastasis. Greater quantities and densities of MetaSites have been shown to correlate to a higher risk of metastasis. A rating scale is used to classify each patient's test results as low, medium, or high risk.

Importantly, the MetaSite *Breast* test does not require any special equipment, techniques, or procedures, and as such, is designed to be seamlessly incorporated into the standard procedures for analyzing tumor stage and grade.

MetaSite *Breast* has already been validated in two human clinical studies, both of which demonstrated a correlation between MetaSite density and metastases and supported the test's ability to predict systemic, **hematogenous** (resulting from blood-borne tumor cells) metastases. Importantly, the test's ability to predict distant metastasis occurred independently of conventional prognostic indicators, including tumor size, grade, lymph node metastasis, **lymphovascular invasion**, or hormone receptor status.

Additionally, MetaSite *Breast* was evaluated against Genomic Health's Oncotype DX Breast Cancer Assay. In unpublished data, patient samples were classified in high-risk, medium-risk, and low-risk cohorts. The high-risk cohort identified by MetaSite *Breast* was 22 times more likely to experience metastasis than the low-risk group. In contrast, Oncotype DX's high-risk group was only 4.5 times more likely to recur than the low risk group. Based on the study's outcomes, the Company believes that repeating this protocol in a larger study could demonstrate that MetaSite *Breast* supplies valuable information beyond the Oncotype DX test and could become an important element in the clinical care and classification of breast cancer patients.

Ongoing Large-Population Validation Study in Breast Cancer Patients

MetaStat is currently nearing the completion of a validation study of 500 patient tissue samples with two sponsored research partners: the Albert Einstein College of Medicine and Weill Cornell Medical College. The retrospective study, in which the patient follow-up time is a minimum of five years, is being performed on previously collected human cancer tissue samples that have accompanying patient medical histories. The study is designed to further examine the relationship between the MetaSite count at initial diagnosis of invasive **ductal carcinoma** (the most common type of breast cancer) and the patient's risk of systemic metastasis, based on their tissue sample. Once the Company collects the data from the study, MetaStat expects to also gain access to tissue samples that have been tested with Oncotype DX in order to perform a direct comparison of the two assays. MetaStat anticipates that results from its test may not correlate with Oncotype DX results, potentially providing complementary information to physicians in addition to Genomic Health's recurrence score.

MetaStat anticipates that data from this trial will likely be available in the first half of 2013. If results demonstrate a similar predictive ability to the previous 44- and 60-patient studies, the Company could begin pilot marketing the MetaSite *Breast* test as early as the second half of 2013. Greater details relating to MetaStat's marketing and commercialization strategy are provided on pages 32-35.

The Company's MenaCalc™ Diagnostic Platform

A number of genes have been identified that must be up- or down-regulated in invasive tumor cells in order to cause metastasis. Several researchers behind MetaStat's technologies determined that one of the key upregulated genes encodes the protein **Mena**. In most individuals, Mena is only present in developing embryos where the protein supports nervous system branching, and becomes scarce and undetectable in healthy adults. However, Mena can reappear in cancer cells, where it supports cancer **invasion** and metastasis.

In cancer cells, Mena proteins can occur in several forms (called "**isoforms**" or "splice variants"). Two isoforms of Mena are up-regulated in invasive tumor cells (designated ⁺⁺ and ⁺⁺⁺) while one type ("11a") is down-regulated in these highly metastatic cells (Source: *Clinical & Experimental Metastasis* 2009; 26:125-159). The Mena⁺⁺⁺ isoform is called Mena^{INV} due to its effects of increasing tumor invasion and metastasis, including metastasis to the lung (Source: *Developmental Cell* 2008; 15[6]:813-28). Two different rodent models have shown that levels of Mena^{INV} were three to four times higher in invasive cells versus primary tumor cells (Source: *Developmental Cell* 2008; 15[6]:813-28).

This research is the foundation for MetaStat's MenaCalc diagnostic technology platform, which seeks to determine individual expression levels of the Mena isoforms using a biopsy of cancer tissue. After extraction from the patient, tumor cells are evaluated for the presence and ratio of the noninvasive Mena 11a isoform to the invasive Mena^{INV} isoform. The relationship between Mena 11a and Mena^{INV} is measured via a "MenaCalc Metastasis Score," which may ultimately be used to create an individual metastatic profile as early on in disease progression as possible. Additionally, a patient's Mena isoform profile could be documented over time to identify trends and detect stability or progression of the disease as well as to detect the efficacy of various therapies in real time.

MetaStat is developing three product candidates based on the MenaCalc platform: (1) MenaCalc *Breast*; (2) MenaCalc *Lung*; and (3) MenaCalc *Prostate*. The Company reports that research to date in breast cancer has illustrated a correlation between the MenaCalc *Breast* Metastasis Score and the MetaSite *Breast* Metastasis Score, which has been confirmed in an 797-patient study conducted at the Yale University School of Medicine, Albert Einstein College of Medicine, and MIT, the results of which have been published (Source: Agarwal, S., Gertler, F., Balsamo, M., Condeelis, J., Camp, R., Xue, X., Lin, J., Rohan, T., Rimm, D. "Quantitative Assessment of Invasive Mena Isoforms (MenaCalc) as an Independent Prognostic Marker in Breast Cancer." *Breast Cancer Research* 2012; 14[5]: R124). MetaStat subsequently aims to initiate a 550- to 1,000-patient validation study of the MenaCalc *Breast* test.

Data collected in lung **adenocarcinoma** and prostate tumors have also shown the ability of MenaCalc to predict cancer spread. A 70-patient study has been completed in lung adenocarcinoma at the Yale University School of Medicine, Albert Einstein College of Medicine, and MIT, and has been reported to have promising preliminary data showing the ability to predict survival (Source: MetaStat's Form 10-K filed with the SEC on June 13, 2012). As well, having completed a favorable pilot study at MIT for a MenaCalc *Prostate* test, MetaStat is now planning a larger, confirmatory trial for the MenaCalc *Prostate* candidate.

MenaBloc™ Platform: Potential Therapeutic Targets for Metastatic Cancer

To MetaStat's knowledge, there is not yet an approved therapy that specifically targets metastasis. Possibly due to characteristics of metastatic cells that make them resistant to many therapies, current treatment for metastatic cancer is similar to, but more aggressive, than that used to combat the growth of primary tumors (e.g., chemotherapy and **radiation therapy**). The primary goal of these treatments is to control tumor growth or to relieve symptoms. While treatments may help prolong life, metastatic disease remains the chief reason why cancer patients succumb to their disease, accounting for approximately 90% of cancer fatalities (Source: CancerQuest, Emory University's cancer education and outreach program, October 2011). Thus, there is a significant unmet need for therapies that are based on a solid understanding of the process of metastatic disease, including techniques to kill or stop the spread of metastatic cancer cells or to disrupt individual steps in the metastatic process.

MetaStat's preclinical pipeline includes screening for a therapeutic molecule designed to inhibit the Mena^{INV} protein, which the Company believes could be the first product approved to preemptively eliminate or reduce metastasis. The MenaBloc platform is based on research conducted by the Licensors. In preclinical testing, mice that were both genetically predisposed to highly metastatic breast cancer and unable to produce the Mena protein developed breast cancer tumors, but no metastatic tumors, unlike Mena-producing mice controls (Source: Roussos et al., *Breast Cancer Research* 2010, 12:R101). Greater details of the preclinical research supporting the development of a Mena inhibitor are provided on pages 19-26. MetaStat intends to begin screening candidate molecules in 2013 as part of its MenaBloc therapeutic platform.

Corporate Information

MetaStat, Inc. was incorporated in Texas in 2009 and re-incorporated in Delaware in 2010. In February 2012, the Company was wholly acquired by Photovoltaic Solar Cells, Inc., a **blank check company** with limited assets (other than cash) and operations. Photovoltaic subsequently changed its name to MetaStat, Inc. (incorporated in Nevada) and changed the name of its new Delaware subsidiary company to "MetaStat BioMedical, Inc." The Company trades as "MTST" on the Over-the-Counter Bulletin Board (OTC.BB).

Headquarters and Employees

MetaStat has principal executive offices in Montclair, New Jersey. The Company has three employees: (1) Oscar L. Bronsther, M.D., F.A.C.S., the Company's chief executive officer and chief medical officer; (2) Mr. Warren C. Lau, MetaStat's president and chief financial officer; and (3) Daniel Schneiderman, the Company's vice president of finance, comptroller, and secretary. Biographies for these individuals are provided on page 11.

MetaStat also has relationships with 19 medical doctors, scientists, and engineers—nearly half of whom are on a consulting basis. The remaining individuals are full-time researchers funded by MetaStat’s research and development collaborations. This staff is performing the Company’s large-population validation study for *MetaSite Breast* at the Albert Einstein College of Medicine, Weill Cornell Medical College, and MIT, and studies using *MenaCalc* for breast and lung at the Albert Einstein College of Medicine, MIT, and Yale University. The Company is currently evaluating institutions and companies to screen for potential candidate compounds to develop a *MenaBloc* therapeutic, and expects this initiative to commence within 12 months.

Growth Strategy

MetaStat seeks to build a commercial-stage life science company operating in the cancer diagnosis, prognosis, and treatment field. To do so, the Company has identified several initiatives that it believes can further this objective.

One of the Company's chief objectives is to continue to innovate and advance its proprietary technology through the completion of clinical studies that confirm the years of scientific research that have gone into developing MetaStat's platforms. As pivotal trials are completed, the Company plans to undertake sales and marketing efforts targeted at the oncology community. Page 34 details MetaStat's planned pilot-stage marketing program and subsequent full-scale marketing proposal for the MetaSite *Breast* test, which could become commercially viable during 2013. A crucial aspect of MetaStat's commercialization plan entails pursuing third-party reimbursement (from private parties, Medicaid, and Medicare) for its products.

Following the development of the MetaSite platform for breast cancer, MetaStat expects to expand the technology into additional cancer indications as well. Likewise, the Company's growth strategy also includes finalizing confirmatory studies of MenaCalc and MenaBloc candidates in order to move multiple products into sales and marketing.

Operationally, MetaStat is working to expand into other countries outside of the U.S., such as Canada and Europe. The Company already holds rights to patent applications in Canada and Europe, as well as the U.S. As operations ramp-up and move from the research stage to product launch, MetaStat will likely need to attract and retain additional skilled personnel, establish and maintain clinical reference laboratory accreditations (in order to analyze and distribute results to physicians from its diagnostic tests), and obtain patents for the underlying technologies and products.

Potential Milestones

MetaStat has identified several corporate milestones (as listed below) that it aims to achieve within the next 12 to 24 months as the Company prepares to launch its first diagnostic product, MetaSite *Breast* (pending results of the ongoing validation study).

- Obtain results from the 500-patient, MetaSite *Breast* validation study in the first half of 2013
- Prepare for the commercialization of MetaSite *Breast* test, including a laboratory build-out
- Commence pilot marketing of the MetaSite *Breast* diagnostic test as early as the second half of 2013
- Launch a full marketing program for MetaSite *Breast* in 2014
- Initiate additional validation studies for MenaCalc (indications to be determined)
- Begin screening candidate molecules for the MenaBloc therapeutic platform
- Explore license/joint venture opportunities for MenaBloc

Intellectual Property

Patent protection is a core component of MetaStat's business, as the Company believes broad coverage is essential as the field for metastasis treatment evolves and expands. MetaStat seeks domestic and international coverage for its technologies, and invests in qualified patent counsel. Much of MetaStat's current intellectual property is held under a license agreement with the Albert Einstein College of Medicine of Yeshiva University, MIT, Cornell University, and the IFO-Regina Elena Cancer Institute, as described below. The Company's portfolio spans 15 years of research through these institutions.

Key Technology License Agreements

The platform technology employed by MetaStat for analyzing tissue samples, among other sponsored research initiatives, was initially developed by a consortium of scientific institutions. The Company licensed rights to the technology from these institutions in August 2010 under a Patent and Technology License Agreement.

Altogether, the August 2010 license agreement served to provide MetaStat with global, exclusive rights to materials and methods developed by the institutions for use in diagnosing and treating the metastasis of solid tumor cancers. It covered pending patent applications, patent disclosures, cell lines, and technology associated with understanding the underlying mechanisms of metastasis in solid tumor epithelial cancers. In exchange, MetaStat issued equity to the licensors, reimbursed them for patent expenses, agreed to pay future patent expenses, annual license maintenance fees, and future royalties and milestone payments.

Subsequently, MetaStat also entered into a Sponsored Research Agreement with the Albert Einstein College of Medicine and Weill Cornell Medical College in April 2011. This agreement entailed a 500-patient, large-population validation study of the MetaSite *Breast* test, for which final payments to both colleges were made in September 2012. This study, which is ongoing, is described on pages 31-32.

In March 2012, MetaStat licensed additional pending patent applications, patent disclosures, cell lines, and related technology from the Albert Einstein College of Medicine. These patent rights were obtained via two license agreements between MetaStat and the College, both made effective in March 2012. Financial terms are similar to the initial agreement in August 2010, and include reimbursement of patent expenses, license maintenance fees, royalties, and milestone payments.

The agreements provide drug developers at MetaStat and potential corporate partners with tools to develop the next generation of anti-metastatic drugs, an artificial blood vessel technology to isolate, collect, genetically profile, and determine chemotherapeutic resistance of a pure population of metastatic cancer cells from a tumor, as well as includes a license to a patent that describes the actual causative gene signature of metastatic cells.

Figure 1 (page 10) summarizes the intellectual property to which MetaStat has received exclusive global rights as a result of the above agreements.

Notices of Allowance Received

In July 2012, MetaStat received Notices of Allowance for patent applications #11/659,514 (U.S.) and #05807467.5 (Europe), which cover methods to recover pure populations of highly metastatic cells, their gene expression profile, and materials/methods to evaluate response to chemotherapy. Notices of Allowance entail written communication from patent authorities that the Company's patents are allowable. The communication specifies the amount of issue and/or publication fees that are due within three months in order to complete the patent registration process (Source: USPTO). This is a key milestone for MetaStat.

Figure 1

PATENT APPLICATION SUMMARY

Jurisdiction	Title	Type and Number
U.S.	Tumor microenvironment of metastasis (TMEM) and uses thereof in diagnosis, prognosis, and treatment of tumors	Provisional Patent Application #61/276,263
U.S.	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	Continuation-in-part of PCT/US08/1343
U.S.	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	Patent Application #12/462,324
U.S.	Isolation, gene expression, and chemotherapeutic resistance of motile cancer cells	Patent Application #11/659,514
U.S.	Human invasion signature for prognosis of metastatic risk	Provisional Patent Application (pending)
U.S.	An in vivo quantitative screening test for anti-metastasis treatment efficacy	Patent Application #12/998,237*
Europe	Isolation, gene expression, and chemotherapeutic resistance of motile cancer cells	European Patent Application #05807467.5
Europe	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	European Patent Application #08713370.8
Canada	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	Patent Application #2,676,179
Canada	Isolation, gene expression, and chemotherapeutic resistance of motile cancer cells	Patent Application #2,576,702

* Based on PCT International Patent Application PCT/2009/005851.

Source: MetaStat, Inc.

Trademarks

MetaStat has received a Notice of Allowance in the U.S. for the “MetaStat” trademark and the Company logo, and seeks additional trademark protection for the following terms: MetaSite, MetaSite *Breast*, MenaCalc, MenaCalc *Breast*, MenaCalc *Lung*, MenaCalc *Prostate*, and MenaBloc.

Company Leadership

Management and Scientific Advisory Board

Figure 2 summarizes MetaStat's key management team members, followed by brief biographies.

Figure 2
MANAGEMENT

Oscar L. Bronsther, M.D., F.A.C.S.	Chief Executive Officer, Chief Medical Officer, and Director
Warren C. Lau	Founder, President, Chief Financial Officer, and Director
Daniel H. Schneiderman	Vice President of Finance, Comptroller, and Secretary

Source: MetaStat, Inc.

Oscar L. Bronsther, M.D., F.A.C.S., Chief Executive Officer, Chief Medical Officer, and Director

Dr. Bronsther is a diplomat, American Board of Surgery, and is the chairman, Section of General Surgery, at Inova Fairfax Hospital. He is also a clinical professor of surgery at George Washington University in Washington, D.C. From 2005 to 2007, he served as chairman of the Board of National Transplant Network. Dr. Bronsther received a B.A. from the University of Rochester in 1973, an M.D. from Downstate Medical Center in 1978, was a Fellow in Kidney Transplantation at Downstate Medical Center, and was a Fellow in Liver Transplantation at the University of Pittsburgh Center. Dr. Bronsther's editorial positions include reviewer, Journal of the American College of Surgeons, Transplantation, Transplant Proceedings, Liver Transplantation and Surgery, and American Journal of Kidney Disease. Dr. Bronsther is the author of 63 peer-reviewed publications, seven books and book chapters, and has participated in over 30 invited lectures.

Warren C. Lau, Founder, President, Chief Financial Officer, and Director

Mr. Lau is MetaStat's founder, president, chief financial officer, and a director. He also served as chief executive officer (CEO) from the Company's formation in July 2009 through December 2012. From October 2005 to March 2008, Mr. Lau served as a director and as the founder, president, and CEO of HoustonPharma, Inc. Previously, he was the president and CEO as well as a director of Opexa Therapeutics (OPXA-NASDAQ), which formed as a result of the acquisition of Opexa Pharmaceuticals by PharmaFrontiers Corp., a company founded by Mr. Lau in February 2003. Mr. Lau was the founder of Adventrx Pharmaceuticals, Inc. (ANX-NYSE MKT) in 1996. He served as its president and CEO and as a member of its Board of Directors from July 1996 through November 2001. During his time as president and CEO, Adventrx consummated two acquisitions, including Biokeys Pharmaceuticals, Inc. and Immune Complex Corporation, which was later spun off to shareholders. From November 1997 to September 1998, Mr. Lau served as a director of Immune Complex Corporation and Synthetic Genetics, Inc., both privately held biotechnology companies.

Daniel H. Schneiderman, Vice President of Finance, Comptroller, and Secretary

Mr. Schneiderman has served as MetaStat's vice president and comptroller since February 27, 2012. He was appointed vice president of finance in December 2012. Mr. Schneiderman has 10 years of investment banking and corporate finance experience. He has focused on private and public equity for small/mid-market capitalization companies mainly in the healthcare and life sciences sectors. During his career, Mr. Schneiderman has participated in public and private financings of approximately \$500 million. Prior to joining MetaStat, he was senior vice president of investment banking for Burnham Hill Partners LLC, where he worked since 2008. From 2004 through 2008, Mr. Schneiderman was vice president of investment banking at Burnham Hill Partners, a division of Pali Capital, Inc. Previously, he worked at H.C. Wainwright & Co. in 2004 as an analyst. Mr. Schneiderman holds a Bachelor's degree from Tulane University.

Board of Directors

MetaStat's Board of Directors oversees the conduct of and supervises the Company's executive management team. Figure 3 provides a summary of Board members, followed by brief biographies. The appointments of Mr. David Siegel, Dr. Patrick Mooney, and Mr. Johan Spoor to MetaStat's Board of Directors became effective in April 2012. Mr. Spoor was appointed chairman of the Board in December 2012.

Figure 3
BOARD OF DIRECTORS

Johan M. (Thijs) Spoor, MBA	Chairman of the Board
Oscar L. Bronsther, M.D., F.A.C.S.	Chief Executive Officer, Chief Medical Officer, and Director
Warren C. Lau	Founder, President, Chief Financial Officer, and Director
David N. Siegel	Director
Patrick T. Mooney, M.D.	Director

Source: MetaStat, Inc.

Johan M. (Thijs) Spoor, MBA, Chairman of the Board

Mr. Spoor has been CEO, president, CFO, and director of FluoroPharma Medical Inc. (FPMI-OTC), a biopharmaceutical company, since May 2011. He holds a nuclear pharmacy degree from the University of Toronto as well as an MBA from Columbia University with concentrations in finance and accounting. Mr. Spoor has been a guest lecturer at Columbia Business School, Kings College in London, and the University of Newcastle in Australia. Mr. Spoor was previously CFO for Sunstone BioSciences, Inc. from February 2010 through September 2010. Prior to joining Sunstone, he worked as a consultant at Oliver Wyman from December 2008 through February 2010, focusing on helping pharmaceutical and medical device companies evaluate global revenue potential in the face of complex regulatory approvals, the reimbursement environment, and the impact of physician preference within constantly evolving standards of care. He further specialized in the implications of healthcare reform on new product approval and health insurance reform. Mr. Spoor has also been an equity research analyst at J.P. Morgan from July 2007 through October 2008 and Credit Suisse from November 2005 through July 2007 covering the biotechnology and medical device industries. Prior to his career on Wall Street, Mr. Spoor worked in the pharmaceutical industry, spending 11 years with Amersham plc/GE Healthcare, where he worked in seven countries in a variety of roles, including setting up Good Manufacturing Practice (GMP) facilities, accountability for the nuclear cardiology portfolio, and as the director of new product opportunities leading the positron emission tomography (PET) strategic plan. Mr. Spoor's background in nuclear pharmacy, finance and accounting, and as a healthcare research analyst, as well as his experience at both large and small healthcare companies, provides him with a broad familiarity of the range of issues confronting a developing biotechnology company.

Oscar L. Bronsther, M.D., F.A.C.S., Chief Executive Officer, Chief Medical Officer, and Director

Biography provided on page 11.

Warren C. Lau, Founder, President, Chief Financial Officer, and Director

Biography provided on page 11.

David N. Siegel, Director

Mr. Siegel was appointed president and CEO of Frontier Airlines, Inc. (part of Republic Airways Holdings Inc. [RJET-NASDAQ]) in January 2012. Previously, he was a managing director of Hyannis Port Capital, Inc. from June 2010 to December 2011. Mr. Siegel served as chairman and CEO of XOJET, Inc., a private aviation company, from October 2008 until May 2010. Before joining XOJET, he was chairman and CEO of Zurich-based Gategroup, AG from June 2004 to March 2009. Mr. Siegel has also served as chairman and CEO of Gate Gourmet Group, Inc., an independent airline catering, hospitality, and logistics company. Prior to Gate Gourmet Group, he was president, CEO, and a member of the Board of US Airways Group, Inc. (LCC-NYSE) and US Airways, Inc., the airline operating unit. Prior to joining US Airways, Mr. Siegel was chairman and CEO of Avis Rent A Car System, Inc. (part of Avis Budget Group, Inc. [CAR-NASDAQ]). His service as a member of senior management and boards of a number of U.S. corporations is expected to provide MetaStat's Board of Directors with significant financial and management experience.

Patrick T. Mooney, M.D., Director

Dr. Mooney currently serves as the CEO, president, and chairman of the Board of Directors of Echo Therapeutics, Inc. (ECTE-NASDAQ), a medical device company, and has held those roles since September 2007, June 2009, and January 2008, respectively. He also previously served as president, CEO, and director of Echo when it was a privately held company (prior to its merger with Sontra Medical Corp.) from September 2006 to September 2007. Prior to joining Echo, Dr. Mooney was president, CEO, and chairman of Aphton Corp., formerly a publicly traded biopharmaceutical company, from January 2004 to November 2006. He served as senior biotechnology analyst at Thomas Weisel Partners, LLC, a full-service merchant banking firm, and as senior biotechnology analyst at Janney Montgomery Scott, LLC, an investment banking firm. He graduated from the Jefferson Medical College of Thomas Jefferson University and trained as a surgical resident at Thomas Jefferson University Hospital. From June to September 2010, Dr. Mooney was a member of the Board of Directors of Quantrix Biomedical Corp. (QTXB-OTC), a healthcare diagnostics company. Dr. Mooney's medical education and experience as a practicing clinician, as well as his industry-specific extensive management experience, is believed to provide him with a broad and deep understanding of the science underlying MetaStat's business and its competitors' efforts, which is a favorable resource for the Company's Board of Directors.

Scientific and Clinical Advisory Board

The Company's scientific team includes several individuals who have held key roles in the supporting research behind MetaStat's platform technologies over the past 15 years.

John S. Condeelis, Ph.D., Chairman of the Scientific Advisory Board

Dr. Condeelis is professor and co-chair of anatomy and structural biology and co-director of the Gruss Lipper Biophotonics Center, and the Judith and Burton P. Resnick Chair in Translational Research at the Albert Einstein College of Medicine. He is also the scientific director of the Analytical Imaging Facility at the Albert Einstein College of Medicine as well as the director of the Tumor Microenvironment and Metastasis Program at the Albert Einstein Cancer Center. Dr. Condeelis is a pioneer in developing microscope techniques for use in intravital imaging—observing the behavior of cells in living animals. His work has led to a clinical test of biopsy tissue to determine whether a woman's breast cancer will spread, which could help determine treatment. Dr. Condeelis and colleagues licensed the patent rights for the breast cancer assay to MetaStat. A fellow of the American Association for the Advancement of Science, Dr. Condeelis is the recipient of the Allen Foundation Scholar Award and the Hirschl Career Scientist Award. He has served on numerous study sections of the National Institutes of Health and the American Cancer Society, as a consultant to the National Cancer Institute, and on the editorial boards of several prominent journals, including the *Journal of Cell Biology*.

Frank B. Gertler, Ph.D.

Dr. Gertler is a professor of biology at the Koch Institute for Integrated Cancer Research, part of MIT. He received a Ph.D. in 1992 from the University of Wisconsin, Madison. He has been presented with the following honors: the American Society for Cell Biology's Early Career Life Scientist Award (2003), the W.M. Keck Foundation's Distinguished Young Scholars in Medical Research Award (2000), and the McKnight Endowment Fund for Neuroscience's McKnight Scholar Award (2000).

Joseph Sparano, M.D.

Dr. Sparano is professor of medicine and obstetrics, gynecology, and women's health at the Albert Einstein College of Medicine. Additionally, his other positions held include associate chairman of the Department of Oncology at Montefiore Medical Center; associate chair for disease-oriented research at Eastern Cooperative Oncology Group (ECOG); chair of the ECOG Breast Cancer Committee; member of the National Cancer Institute Investigational Drug Steering Committee, Breast Cancer Steering Committee, and Lymphoma Steering Committee; and study chair of TAILORx (Trial Assigning Individualized Options for Treatment), the first National Cancer Institute-sponsored trial integrating a gene expression assay in clinical decision making.

Joan Jones, M.D.

Dr. Jones is a well-known clinical surgical pathologist and co-inventor of the MetaSite test. Currently, she is professor of clinical pathology and laboratory medicine at Weill Cornell Medical College. She is a past president of the Leo M. Davidoff Society and the New York Pathological Society. Dr. Jones has held major administrative positions, including deputy director of anatomic pathology, Einstein Hospital, and director of surgical pathology, Einstein Division, Montefiore Medical Center, and director, anatomic pathology, New York Presbyterian Hospital/Cornell. Dr. Jones has extensive clinical experience in breast pathology and a longstanding interest in the contribution of cell migration and the microvasculature to metastatic progression. She led the pathology team in the development and validation of the MetaSite test.

Thomas E. Rohan, M.D., Ph.D.

Dr. Rohan is a cancer epidemiologist who studies the role of genetic/molecular, nutritional, and hormonal factors in the etiology and pathogenesis of a wide range of cancers. Much of his work has focused on breast cancer, where he has a particular interest in the molecular pathogenesis of breast cancer. His work focuses on identifying molecular changes in benign breast disease tissue that predispose to the development of subsequent breast cancer. Many of his other studies have involved cohort investigations, mostly within the Women's Health Initiative cohorts, the Canadian National Breast Screening Study dietary cohort, and more recently within a new cohort that he established, the Canadian Study of Diet, Lifestyle, and Health. He has published scientific articles on cancer epidemiology, and he has co-edited books on cancer precursors and on cervical cancer. In addition to being chair and a professor of the Department of Epidemiology and Population Health, Dr. Rohan is associate director for population sciences in the Albert Einstein Cancer Center, a member of the Board of Scientific Counselors of the National Cancer Institute, and the Atran Foundation's Chair in Social Medicine. He is on the editorial board of several journals, and is a member of several professional societies.

Core Story

Tumor metastasis (or “spread”) and especially hematogenous (blood borne) metastasis is the leading cause of cancer-related morbidity and mortality, yet treatments today are focused on attacking cancer cells without adequately disrupting the mechanisms causing tumors to migrate throughout the body. While in some cases, cancer treatments help prolong life, accumulating evidence has demonstrated that traditional therapies are not only inadequate to combat metastatic disease but may also be harmful over the long term (Source: *European Journal of Cancer* 2010; 46:1177-1180). Complicating this issue is a lack of definitive, objective tools to determine whether or not a tumor is likely to spread, which can result in under- or over-treatment. MetaStat, Inc. (“MetaStat” or “the Company”) strives to improve disease management for a variety of common cancers by developing and ultimately seeking to commercialize improved diagnostic/prognostic tools targeted for the early detection of metastatic disease. Capitalizing upon its proprietary science, MetaStat further aims to launch next-generation therapeutics optimized for the prevention or treatment of metastatic cancer.

MetaStat’s product pipeline is divided into three unique platforms.

- **MetaSite™:** A diagnostic platform to predict the likelihood of cancer spreading based on the density of “MetaSites” (three-cell structures: a macrophage, carcinoma cell, and epithelial cell) in tumor tissue samples
- **MenaCalc:** A diagnostic platform to predict metastasis using measurement of the relative levels of Mena protein isoforms in a tumor sample
- **MenaBloc:** A technology to potentially create therapeutic molecules that inhibit Mena and treat metastasis

MetaStat anticipates that its technologies may ultimately be applicable to all epithelial solid tumor cancers, which represent over 80% of cancer cases. This includes four of the five largest cancer indications—breast, prostate, lung, and bowel cancers—as well as tumors in the pancreas, brain, liver, or head and neck.

The Company believes that its diagnostic tests and therapeutic candidates, as overviewed on the accompanying pages, can improve treatment efficacy and lower the costs associated with evaluating and treating severe cancers. Its platform technologies are licensed from the Albert Einstein College of Medicine of Yeshiva University, the Massachusetts Institute of Technology (MIT), Cornell University, and the IFO-Regina Elena Cancer Institute (collectively, the “Licensors”). They are supported by over 15 years of research, highlights of which are detailed on pages 19-26.

Figure 4 lists several academic achievements that have been instrumental in the development of MetaStat’s platform technologies, such as the discovery of the mechanism of metastasis, which was made possible by new tools that the Licensors developed to observe and isolate metastatic cancer cells. MetaStat believes that its technologies and corresponding product candidates hold a competitive advantage because they are based on direct microscopic observation of the mechanisms/behaviors of metastatic cells in living, human-derived tumors.

Figure 4

NOTABLE ACHIEVEMENTS BY METASTAT’S RESEARCH TEAM IN THE FIELD OF METASTASIS

- Invented and patented an Intravital Imaging Window that is used in conjunction with multiphoton microscopy to directly observe how metastatic cells move inside a tumor
- Invented and patented an artificial blood vessel that enables researchers to attract a genetically discrete population of highly metastatic cells, thus enabling them to describe the gene signature characteristic of high metastatic potential
- Was first to discover and explain how and why metastatic cells are attracted to blood vessels
- Discovered by direct visual observation the micro-anatomical site, the “window” in the blood vessels, that metastatic cells squeeze through to enter the bloodstream to begin their journey

Source: MetaStat, Inc.

Cancer Metastasis Overview

Cancer—a group of complex diseases characterized by uncontrolled growth of abnormal cells and the formation of malignant tumors—is a significant health concern globally. Treating cancer can be a lengthy and costly process, complicated by a number of side effects for the patient. Each type of cancer responds differently to treatments depending on the individual and the type and location of the cancer. Millions of people are living with cancer or have been diagnosed with the disease. Cancer was responsible for 7.6 million deaths worldwide in 2008 (the most recent year for which data was available from the World Health Organization). Currently, it remains the second leading cause of death in the U.S., behind heart disease. The American Cancer Society (ACS) estimates that approximately half of all men and one-third of all women will develop cancer during their lifetimes in the U.S.

Cancer is also quite costly to treat. In 2010, cancer-related medical costs were expected to reach nearly \$125 billion, with breast cancer representing the largest portion of these costs at \$16.5 billion. By 2020, costs are expected to reach \$158 billion (in 2010 dollars), a more than 27% increase over 2010 costs (Source: the National Institutes of Health, January 12, 2011).

Cancer Metastasis

Metastasis is the process by which cancer spreads from its original location to other parts of the body, developing what is known as a metastatic tumor that has the same type of cancer cells as the original (or “primary”) cancer. Metastatic cancer is responsible for approximately 90% of cancer fatalities (Source: CancerQuest, Emory University’s cancer education and outreach program, October 2011). Virtually all types of cancer—including cancers of the blood and the **lymphatic system** (e.g., leukemia)—can result in metastatic tumors.

Cancer cells are capable of spreading to numerous locations in the body. Figure 5 identifies likely sites of metastasis for various cancer types. Most frequently, cancer metastasizes to the lungs, bones, and liver. Metastatic cancer is given the same name as the location of the primary tumor (e.g., breast cancer that spreads to the lungs and forms a new tumor is called metastatic breast cancer). Metastatic cancer cells generally have the same appearance under a microscope as cells of the primary tumor and typically have some molecular features in common.

Figure 5
MAIN SITES OF METASTASIS BY CANCER TYPE

Cancer Type	Main Sites of Metastasis	Cancer Type	Main Sites of Metastasis
Breast	Lungs, liver, bones	Pancreas	Liver, lungs, peritoneum
Colon	Liver, peritoneum, lungs	Prostate	Bones, lungs, liver
Kidney	Lungs, liver, bones	Rectum	Liver, lungs, adrenal gland
Lungs	Adrenal gland, liver, lungs	Stomach	Liver, peritoneum, lungs
Melanoma	Lungs, skin/muscle, liver	Thyroid	Lungs, liver, bones
Ovary	Peritoneum, liver, lungs	Uterus	Liver, lungs, peritoneum

Source: National Cancer Institute.

Four of the five most commonly diagnosed cancer types in the U.S.—breast, prostate, lung, and colorectal/bowel cancer—are associated with metastasis.

Progression of Metastatic Cancer

Cancers spread in three ways: (1) local spread or “invasion,” which is growth within the primary site; (2) lymphatic spread, in which tumor cells gain access to lymphatic vessels and spread to regional lymph nodes; and (3) hematogenous metastasis, where cancer cells enter the bloodstream in order to travel to other areas of the body. In order to migrate by this third means, cancer cells extend part of the cell forward and release attachment at the back end. To move past neighboring cells, the tumor cells rearrange their cytoskeleton—the framework of structural proteins inside a cell that gives the cell its shape, flexibility, and **motility**—while attaching to the other cells and the **extracellular matrix** via proteins on the plasma membranes.

In the process of migration, cells may encounter a thin layer of proteins and **glycoproteins**, called the basement membrane, which prevents further movement. The basement membrane is a protective barrier that underlies the epithelium, which lines the cavities and surfaces of organs (including skin) and the endothelium, which lines the interior surface of blood vessels. Cancer cells secrete various digestive enzymes to degrade the barrier and pass through, creating opportunities for the cells to enter the bloodstream and spread to other areas of the body. Many migrating tumor cells die in the process by getting damaged or stuck in the blood vessel, or they may be recognized and destroyed by the immune system, among other reasons. Some cells arrive at a new location, but do not multiply sufficiently to form a tumor or may lay dormant for years before beginning to grow again. Nevertheless, a small percentage of cells may settle and begin to form a new tumor.

Treatment for Metastatic Cancer

Preventing or reducing metastasis is a critical component of successfully treating cancer and decreasing the number of cancer-related deaths (Source: *European Journal of Cancer* 2010; 46:1177-1180). Yet to MetaStat’s knowledge, there is no therapeutic approved specifically to target metastasis. Currently, treatment for metastatic disease is similar to that used to target primary tumors, and includes chemotherapy, biological therapy, targeted therapy, hormonal therapy, local therapy, surgery (although more rarely for metastatic disease), radiation therapy, or a combination thereof. Treatment depends on the type of cancer as well as the size, location, and number of metastatic tumors, the patient’s age and health, and the therapies used previously. Radiation therapy remains a mainstay of treatment for metastatic tumors, and patients may receive multiple chemotherapy courses. The primary goal of these treatments is to control the growth of the cancer or to relieve symptoms. While treatments may help prolong life, metastatic disease remains a main factor causing cancer patients to succumb to their disease.

The conventional method for treating metastatic tumors centered on the notion that metastases were essentially similar to primary tumors, and thus assumed that traditional methods to control primary tumor growth could also suppress metastatic growth. However, accumulating evidence has demonstrated that traditional growth control approaches are not only inadequate to combat metastatic disease, but may also be harmful in the long term (Source: *European Journal of Cancer* 2010; 46:1177-1180).

Trending Toward Personalized Cancer Therapy

Historically, many cancer therapies have been prescribed to patients without an understanding of how the individual’s body and tumor(s) will react. Some cancer therapies may be more effective for certain patients but currently are prescribed broadly as part of the traditional standard of care. As such, many chemotherapy treatments are considered to be “hit or miss”—effective in some patients but highly ineffective in others. A greater understanding of the tumor’s genetic abnormalities, as well as a profile of the patient’s immune system, could help to identify, on an individual level, more specialized therapies that offer improved efficacy and outcomes while eliminating the use of ineffective treatments that often cause significant side effects.

A number of recent scientific advances—including the ability to decode cancer genes as well as an improved understanding of how therapies work—offer insight into the genetic and molecular factors causing some individuals to respond to particular drugs while others do not. With this essential information, cancer centers, physicians, and researchers seek to develop personalized cancer therapy regimens (where treatments are tailored specifically to a patient based on their individual genes) that improve survival rates as well as quality of life.

Similarly, these advances may improve patient selection for future clinical trials, potentially leading to increasingly successful data and more medicines being approved for cancer treatment.

In addition, scientific advances are improving diagnostic capabilities in the field. In particular, diagnostic tests may be developed to identify high-risk patients in need of aggressive therapy. If test results indicate that the patient has a low risk of progression or metastasis, then the patient can receive a more moderate treatment regimen and be spared the side effects and expense of aggressive treatment.

MetaStat seeks to become an industry leader in the emerging field of personalized cancer therapy by developing a family of diagnostic tests as well as therapeutic treatments, particularly as it relates to addressing cancer metastasis.

MetaStat's Technology Background

Whether the goal is to prevent cancer cells from spreading throughout the body or, for metastatic tumors, to cease further growth and spread, metastasis is a significant challenge in cancer treatment and a leading cause of cancer-related deaths. Furthermore, the process behind metastasis is highly complex and has proven to be challenging to study in the lab. While the invasion, intravasation, and dissemination aspects of metastatic cancer were known, researchers lacked an in-depth understanding of the mechanisms of invasion and migration and the molecular and behavioral phenotypes as well as how to detect these changes and how these changes affect the behavior of cancer cells. It was believed that an improved understanding of what molecules change to enable metastasis and how these changes affect the behavior of cancer cells could be beneficial for various aspects of metastatic cancer treatment, detection, and prognosis.

Developing Novel Tools to Better Understand and Treat Metastatic Cancer

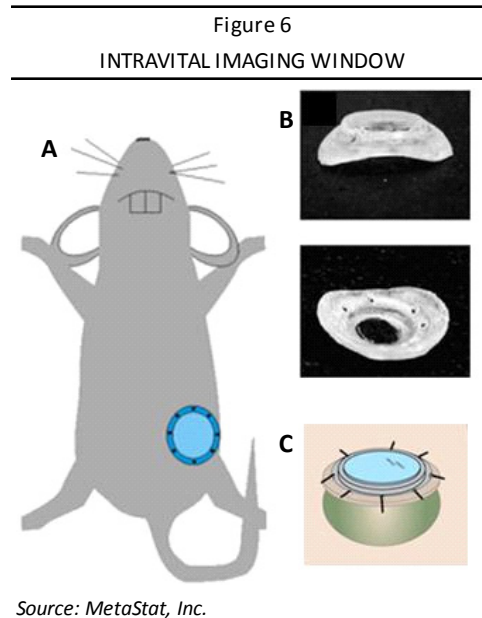
MetaStat's technology is based on over 15 years of research on metastasis and has been developed by researchers in the field at globally recognized institutions. Collectively, the research teams from these institutions (the Licensors) have invented and patented several novel tools to observe the behavior of metastatic cancer cells in tumors, subsequently licensing key rights to MetaStat in order to develop into commercially viable products.

Intravital Imaging Window

Researchers behind MetaStat's technology invented and patented an intravital imaging tool that allows scientists to capture images from within a live animal. The imaging window was used to observe and analyze the mechanisms of invasion for metastatic cancer. The chairman of MetaStat's Scientific Advisory Board, Dr. John S. Condeelis (biography on page 13), has pioneered microscope techniques for use in intravital imaging and currently serves as the scientific director of the Analytical Imaging Facility at the Albert Einstein College of Medicine as well as the director of the Tumor Microenvironment and Metastasis Program at the Albert Einstein Cancer Center.

Conceived by Dr. Condeelis and researchers at the Albert Einstein College of Medicine, the intravital imaging window (illustrated in Figure 6) is used in combination with multiphoton microscopy in living mice to observe metastatic cell movement inside a tumor over a long period. The tool was first featured in an article published in *Nature Methods* in December 2008 (Source: *Nature Methods* 2008; 5(12):1019-21).

Once the imaging window was implanted, a multiphoton microscope captured focused images of optically marked cells within the tumor. Multiphoton microscopy employs multiple light sources at various angles and offers key advantages, such as the ability to obtain three-dimensional images as well as images from within live tissue.



Using the Imaging Window In Vivo to Observe Critical Components of Cancer Metastasis

Using a combination of multiphoton-based intravital imaging and microarray-based expression profiling, researchers have been able to identify patterns of gene expression that relate to tumor cell behavior in vivo (within a living organism). In 2007, a study completed by the Albert Einstein College of Medicine, including Dr. Condeelis, capitalized on these technologies to evaluate a mouse model of breast cancer that resembles human breast cancer in both morphology and progression. For the first time, researchers used images to observe cell behavior, particularly the elements that lead to invasion and metastasis, in tumors developed directly from the mammary epithelium in transgenic animals.

Despite having different genetic origins, the invasive tumor cells in both **polyoma middle T oncogene (PyMT)**-derived mouse mammary tumors and cell line-derived tumors exhibited similar changes in gene expression and cell behavior that enabled them to invade surrounding tissue and enter blood vessels—characteristics that differentiate these cells from the general tumor cell population. Invasive cells from the PyMT tumor were shown to be non-dividing, non-apoptotic, chemotherapy-resistant, and **chemotactic**, which is similar to previous findings of mammary tumors derived from the rat MTLn3 cell line (Source: *Cancer Research* 2007; 67(8):3505-11). The invasive tumor cells moved individually and more quickly than seen in vitro (in a test tube, petri dish, etc.) and were polarized toward blood vessels. Changes in gene expression of invasive cells were observed for the Arp2/3 complex, capping protein, and cofilin pathways, as has been seen with prior cell line-derived tumors.

Importantly, invasive tumor cells of various genetic origins and histologic phenotypes have exhibited the same strategy for chemotaxis to **epidermal growth factor (EGF)**. As well, different genes in the same pathway can be altered to achieve an equivalent phenotype. As such, these findings suggest that the invasive and metastatic phenotype of the tumor is determined by the activity of the pathway as a whole rather than a change in expression of any one particular gene. Thus, these pathways represent potential targets to treat tumor cell invasion and metastasis (Source: *Cancer Research* 2007; 67(8):3505-11). In particular, the cofilin pathway has been shown to affect the invasive and metastatic characteristics of tumor cells, and could represent a potential therapeutic target against metastasis (Source: *Nature Reviews Cancer* 2007; 7:429-440).

Discovery of the Micro-anatomical Site that Leads to Metastasis

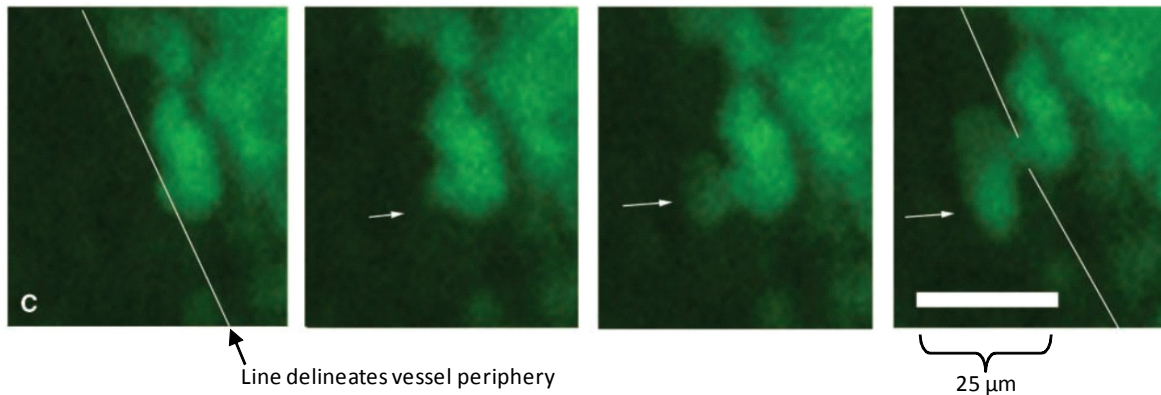
It was long thought that macrophages congregate in tumors to attempt to perform some of the immune system functioning to get rid of foreign cancer cells. However, researchers have learned that cancer has co-opted this process and turned the macrophages into helper cells that help facilitate metastatic movement of cells (Source: *Cancer Research* 2004; 64:7022-7029). Researchers behind MetaStat's licensed technology, including Dr. Condeelis, discovered the biochemical signaling that occurs between macrophages and labeled it the "paracrine loop." Macrophage provides EGF to the tumor cell, which in turn provides colony-stimulating factor (CSF) to the macrophage (Source: MIT TechTV's "2009 Koch Institute Symposium - Frank Gertler"). The findings were published in a 2004 *Cancer Research* article entitled, "A Paracrine Loop between Tumor Cells and Macrophages Is Required for Tumor Cell Migration in Mammary Tumors."

The notion that macrophages contribute to, rather than combat, the metastatic process has been further confirmed in preclinical research. While observing invasive cells through the intravital imaging window (described on page 19), researchers behind MetaStat's licensed technology discovered the essential components enabling metastatic cells to enter the bloodstream and metastasize to other areas of the body. Using the intravital imaging window, researchers observed and recorded a metastatic cell and the macrophage being attracted toward one another and linking together. As viewed from a blood vessel within a mouse, researchers watched as a metastatic cell penetrated the wall of the blood vessel and was swept away by the bloodstream.

Figure 7 (page 21) illustrates an invasive tumor cell entering the bloodstream by penetrating a nearby blood vessel.

Figure 7

A TUMOR CELL IS IMAGED INTRAVASATING INTO A BLOOD VESSEL



Source: *Cancer Research* 2007; 67:8.

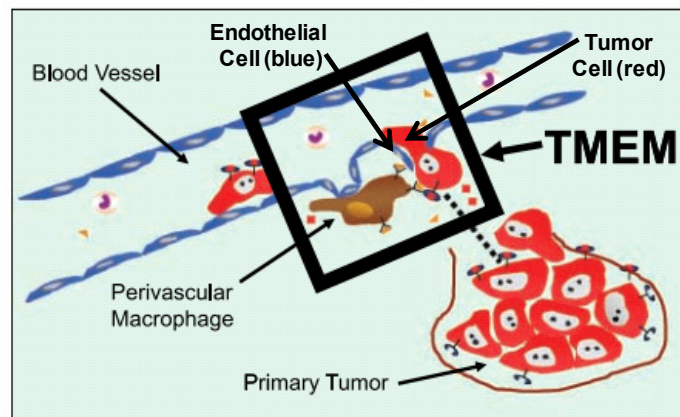
In order to enter a blood vessel (intravasate), three types of cells must present together in the same micro-anatomical site:

- (1) an endothelial cell (a type of cell that lines blood vessels);
- (2) a **perivascular** macrophage (a type of immune cell that guides tumor cells to blood vessels); and
- (3) a tumor cell that produces the Mena protein. (Mena is described on pages 22-26.)

This three-cell structure is shown in Figure 8. This discovery was detailed in *Clinical Cancer Research* in April 2009 and termed by researchers as the Tumor Microenvironment of Metastasis (TMEM). MetaStat refers to this structure as the "MetaSite™." Importantly, researchers have theorized that tumor tissue samples with higher MetaSite density correlate to a higher probability of distant site metastasis. The theory was evaluated in a study of TMEM density human breast carcinoma samples, which is described on pages 29-30. This reasoning serves as the foundation for the Company's MetaSite diagnostic platform and lead product candidate, the MetaSite *Breast* test, as detailed on pages 27-35. This cancer marker is believed to be among the first to reliably predict metastatic outcome in a case-controlled study, and may have potential to dramatically change the approach for breast cancer treatment (Source: Albert Einstein College of Medicine press release, March 24, 2009).

Figure 8

RENDERING OF A TUMOR MACROENVIRONMENT OF METASTASIS (TMEM) OR "METASITE"



Source: *Clinical Cancer Research* 2009; 15(7).

Artificial Blood Vessel

Historically, the unique characteristics of metastatic cells, such as low proliferation combined with a minority presence in tumors, made it difficult to collect useful genetic information with regard to what makes metastatic cells different. The teams who researched MetaStat's technology are believed to be the first to have understood how and why metastatic cells are attracted to blood vessels. This research was published in *Clinical Cancer Research* in April 2009.

With this knowledge, researchers invented and patented an artificial blood vessel—a microneedle filled with chemoattractants that could be used to attract, and thus isolate, a specific population of highly metastatic cancer cells from primary tumors within living animals. Microneedles containing gradients of either epidermal growth factor (EGF) or colony-stimulating factor 1 (CSF-1) were used to collect invasive cells from live primary tumors (Source: Wyckoff et al., *Cancer Research* 2007; 67(6): 7022-7029). These chemoattractants mimicked chemotactic signals from blood vessels and surrounding tissue. To isolate a pure population of metastatic cells, a microneedle with chemoattractant is placed inside a tumor, left for a short period, and then withdrawn. The technology was featured in an article entitled, "Gene expression analysis on small numbers of invasive cells collected by chemotaxis from primary mammary tumors of the mouse" (Source: Wang et al. *BMC Biotechnology* 2003; 3:13).

In July 2012, MetaStat received a Notice of Allowance for U.S. patent application #11/659,514 and European patent application #05807467.5, which describe the artificial blood vessel technology. To the Company's knowledge, this is the first method to effectively isolate, collect, genetically profile, and determine chemotherapeutic resistance of a pure population of metastatic tumor cells. Historically, researchers have been unable to completely isolate metastatic tumor cells, and thus had challenges genetically profiling this population.

Identifying the Invasion Signature for Metastatic Cancer Cells

In order to invade surrounding tissue and metastasize, tumor cells undergo a number of phenotypic changes via various molecular pathways. Seeking to better understand the genetics behind invasive cancer cells, MetaStat's research team designed the artificial blood vessel and various animal models to study these genetic events. Using an artificial blood vessel with EGF, researchers isolated and purified 1,000 metastatic cells to determine the gene signature characteristic of high metastatic potential by comparing the collected metastatic cells to average primary tumor cells. Much of this research is covered in MetaStat's licensed patent application, entitled "Human Invasion Signature for Prognosis of Metastatic Risk."

MetaStat's researchers identified 57 genes of the invasion signature that predict systemic metastasis but not local recurrence, and then narrowed this down to the top 19 genes. The gene signature includes upregulation of Mena and a number of other key regulators of **actin** polymerization and motility. Genes related to apoptosis and cell proliferation were downregulated in invasive cells (Sources: Wang et al., *Cancer Research* 2004; 64: 8585-8594; Wang et al., *Cancer Research* 2007; 67[8]; Patsialou et al., *Cancer Research* 2012 72[8]). As such, conventional chemotherapeutic agents that are designed to interrupt cell division are not effective for these non-dividing cells.

According to MetaStat, this approach is believed to describe the actual causative gene signature of metastatic cells versus currently available technology, which claims to evaluate the risk of cancer recurrence by relying upon correlative mathematical algorithms developed by analyzing whole tumor tissue samples. Importantly, to the Company's knowledge, none of the identified invasion signature genes are detectable by Genomic Health's Oncotype DX test.

Mena Protein and its Role in Cancer Metastasis

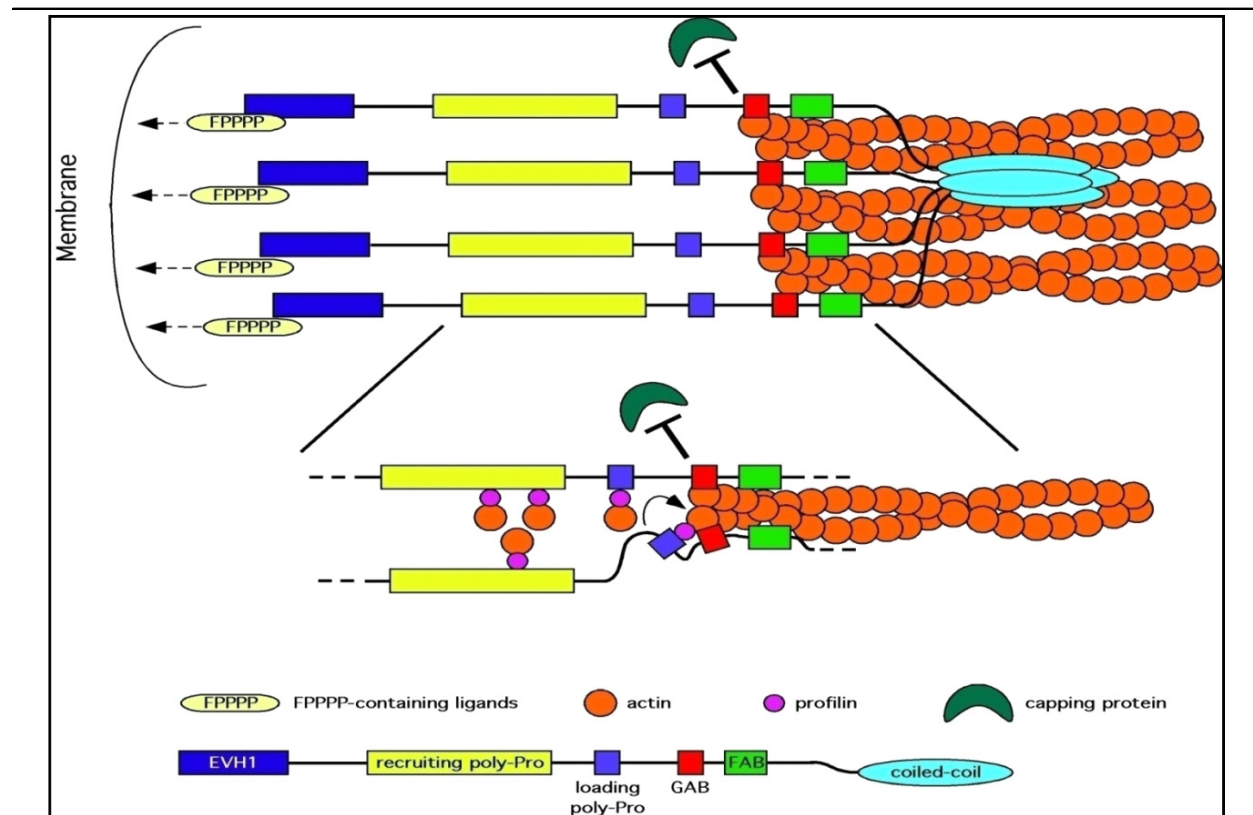
A number of genes have been identified that must be up- or down-regulated in invasive tumor cells in order to cause metastasis. One of the key upregulated genes encodes the protein Mena, which belongs to the vasodilator-stimulated phosphoprotein (VASP) family of proteins. VASP proteins have a role in cell migration (motility) by promoting the assembly of actin fiber networks. Actin fibers form a cellular "skeleton" in the cytoplasm of all cells, and are involved in motion in certain cells types.

The Mena protein is a chief aspect of MetaStat's technology. In most individuals, Mena is only present in developing embryos where the protein supports nervous system branching, and becomes scarce and undetectable in healthy adults. Mena helps embryonic nerve cells, or neurons, organize the formation of axons—nerve fibers that send messages from one neuron to other neurons in the nervous system. In this instance, Mena supports positive and healthy processes and is an essential component in nervous system formation. It is also an important element of cell migration. However, Mena can appear in cancer cells, where it is much more harmful and supports cancer invasion and metastasis by enabling cancer cells to invade surrounding tissues and migrate toward and penetrate blood vessels.

Mena's Function

Figure 9 demonstrates a model of Mena's function as a regulatory protein of the actin network. The growth and elongation of actin fibers is controlled by a process that caps their ends. Mena interferes with (or "antagonizes") the actin capping, allowing the actin fibers to continue to lengthen, protruding the front edge of the cell forward. Greater details concerning the structure and function of the Mena protein are available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3042857>.

Figure 9
MODEL FOR MENA FUNCTION



Sources: MetaStat, Inc. and *Clinical & Experimental Metastasis* 2009; 26:125-159.

Mena's Role in Cancer Metastasis

Mena influences a number of intracellular (inside the cell) signaling programs and serves as part of the pathway that regulates a primary tumor cell's transition to a metastatic cell. Mena has been shown to enhance a cancer cell's ability to invade surrounding tissues in a collaborative study by Dr. Condeelis at the Albert Einstein College of Medicine and Dr. Frank Gertler at the David H. Koch Institute for Integrative Cancer Research at MIT, which was published in *Developmental Cell* in 2008 (Source: Philippar et al., *Developmental Cell* 2008; 15: 813-828). As well, additional information about Mena's role in breast cancer cell cohesion and association with TMEM can be referenced in *Clinical & Experimental Metastasis* (Source: Roussos, E., Goswami, S., Balsamo, M.; Wang, Y.; Stobezki, R.; Adler, E.; Robinson, B.; Jones, J.; Gertler, F.; Condeelis, J.; Oktay, M., *Clinical & Experimental Metastasis* 2011; 28[6]: 515-527).

Mena modulates three elements of migratory behavior in metastatic cancer cells:

- (1) regulation of actin fibers, which affect cancer cell movement and invasion;
- (2) formation of **invadopodia**—specialized membrane **protrusions** that degrade the extracellular matrix and support invasion into surrounding tissues and blood vessels; and
- (3) sensitivity to vascular chemoattractant, which induces the cancer cell to migrate toward blood vessels.

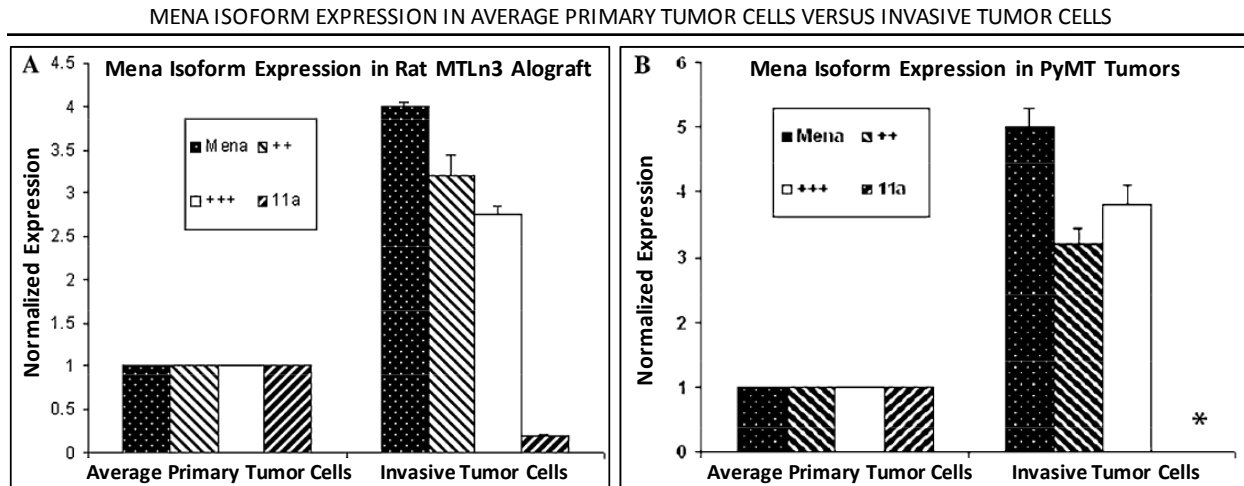
Collectively, these elements support invasion and metastasis. During the process of invasion, continuous degradation of the cellular matrix must occur along the advancing front of the migrating cells, in combination with active cell locomotion. The formation of invadopodia degrades the extracellular matrix, subsequently allowing the tumor cell to send out a well-organized protrusion that invades surrounding tissue and pulls the remainder of the cell behind it. This aspect is largely achieved through Mena's actin fiber regulation. All cells in the human body are able to move due to their actin cytoskeleton, which helps organize the shape of the cell while containing cellular organelles within the cell and in their proper position. However, in metastatic cells, Mena modulates the growth of the leading edge of the cell, allowing actin fibers to continuously grow in one direction and supporting the invasion of cancer cells into other areas of the body. The strength and direction of this invasion is modulated by Mena.

Mena also is responsible for migration of cancer cells toward the vascular system and into other areas of the body. Mena makes cancer cells more sensitive to EGF, which attracts the cells toward blood vessels and is secreted by perivascular macrophages—one of the three cell types that constitute a MetaSite. Thus, metastatic tumor cells are guided to the MetaSite where they are able to gain entry into the blood vessel and spread to other areas.

Expression of Mena in Invasive Tumor Cells

Continued research by MetaStat's university collaborators revealed that, in cancer cells, Mena presents in different varieties (called "isoforms" or "splice variants")—sequences of Mena that have slight structural variations—resulting in more dangerous forms of the Mena protein (Source: *Developmental Cell* 2008; 15[6]:813-828). Small quantities of several Mena isoforms—Mena⁺⁺, Mena⁺⁺⁺, and 11a—are found in average primary tumor cells (APTCs), as shown in Figure 10 (page 25). However, there is a switch in expression when APTCs become invasive. As illustrated in Figure 10, two isoforms of Mena are upregulated in invasive tumor cells (Mena⁺⁺ and Mena⁺⁺⁺), while one type (11a) is downregulated in three different primary mammary tumors, which is consistent with observations in human breast cancers and cancer cell lines (Source: *Clinical & Experimental Metastasis* 2009; 26: 125-159). This pattern continues when invasive tumor cells begin to circulate and metastasize to other areas of the body. Mena expression results a higher ratio of mobile carcinoma cells in vivo, and increases invasive potential both in vitro and in vivo (Source: Philippar et al., *Developmental Cell* 2008; 15: 813-828). The following two scientific journal articles can be referenced for additional information: (1) Roussos et al., *Clinical & Experimental Metastasis* 2011; 28(6): 515-527; and (2) Roussos, E., Wang, Y., Wyckoff, J., Sellers, R., Wang, W., Li, J., Pollard, J., Gertler, F., and Condeelis, J., *Breast Cancer Research* 2010; 12: R101.

Figure 10



Source: *Clinical & Experimental Metastasis* 2009; 26:153-159.

Data collected to date suggest that splicing regulates the activity of Mena during metastasis and a growing body of evidence has implicated alternate splicing events in the progression of cancer. As such, exon-specific antibodies to Mena^{INV} and 11a may be beneficial in identifying tumors with a high risk of invasion, potentially improving the accuracy of diagnosis and prognosis in cancer patients (Source: *Developmental Cell* 2008; 15[6]:813-828).

Animal models were used to evaluate the various effects of Mena isoforms. The most dangerous isoform of Mena is Mena⁺⁺⁺, which has been termed Mena^{INV} due to its potent effects at increasing invasion (in vivo and in vitro) and metastasis, including metastasis to the lung (Source: *Developmental Cell* 2008; 15[6]:813-828). In a study published in 2009, two different rodent models showed that levels of Mena and Mena^{INV} were three to four times higher in invasive cells versus primary tumor cells (Source: Phillipar et al., *Clinical Experimental Metastasis* 2009; 26[2]: 153-159). In animals with Mena^{INV}, there were seven times as many circulating cancer cells in the bloodstream (Source: Roussos et al., *Breast Cancer Research* 2010; 12[6]: R101).

Mena^{INV} also promotes motility in vivo and localizes to the leading edge of motile tumor cells. It further increases the matrix degradation activity of tumor cells as a result of its role in the stabilization of invadopodia, providing opportunities for tumor cells to advance into new territories (Source: *Developmental Cell* 2008; 15[6]:813-828).

Mena^{INV} further increases tumor cells' sensitivity to chemoattractants. Mena^{INV} increases a cancer cell's motility responses stimulated by EGF, the chemical attractant that leads the metastatic cell to blood vessels (Source: *Clinical & Experimental Metastasis* 2009; 26:125-159). In one experiment, Mena^{INV} made metastatic cancer cells 25-times more sensitive to EGF (Source: Phillipar et al., *Developmental Cell* 2008; 15: 813-828). An article in the *Journal of Cell Science* offers intravital images of Mena^{INV}-expressing tumor cells as they migrate toward a blood vessel (Source: Roussos et al., *Journal of Cell Science* 2011; 124: 2120-2131). As well, Figure 11 (page 26) illustrates one of these images as presented in a presentation by Frank Gertler in the 2009 Koch Institute Symposium.

Figure 11

INTRAVITAL IMAGE OF TUMOR CELLS WITH Mena^{INV} INTRAVASATING TOWARD BLOOD VESSELS



GREEN = Tumor Cells with Mena^{INV}

RED = Blood Vessels

Source: MIT TechTV's "2009 Koch Institute Symposium - Frank Gertler."

Resistance to therapies that inhibit the EGF receptor (EGFR) (e.g., Tarceva® and Iressa®) is common in patients with metastatic cancer. Because cells expressing Mena or Mena^{INV} have an increased sensitivity to EGF, researchers have theorized that upregulation of Mena or Mena^{INV} may enable tumor cells to metastasize without the presence of a strong EGF signal, thus escaping the action of these cancer treatments (Source: *Developmental Cell* 2008; 15[6]:813-828).

Mena's Potential as a Biomarker for Metastatic Cancer

The increased expression of Mena^{INV} and decreased expression of 11a in both invasive and metastatic cells could provide opportunities for new diagnostic and prognostic biomarkers to detect the presence of metastatic cancer cells or predict metastatic disease. Recent research has demonstrated the potential of splice variants as cancer biomarkers. As well, analysis of the relative levels of the three isoforms—Mena^{INV}, Mena⁺⁺, Mena 11a—in tumor tissues could be used to create a new ratiometric prognostic marker to predict metastatic risk (Source: *Clinical & Experimental Metastasis* 2009; 26:125-159). As well, an 800-patient study performed to confirm the potential of these changes in expression as biomarkers has been published (Source: Agarwal et al., *Breast Cancer Research* 2012; 14: R124). This concept forms the foundation for MetaStat's MenaCalc diagnostic platform (overviewed on pages 36-37).

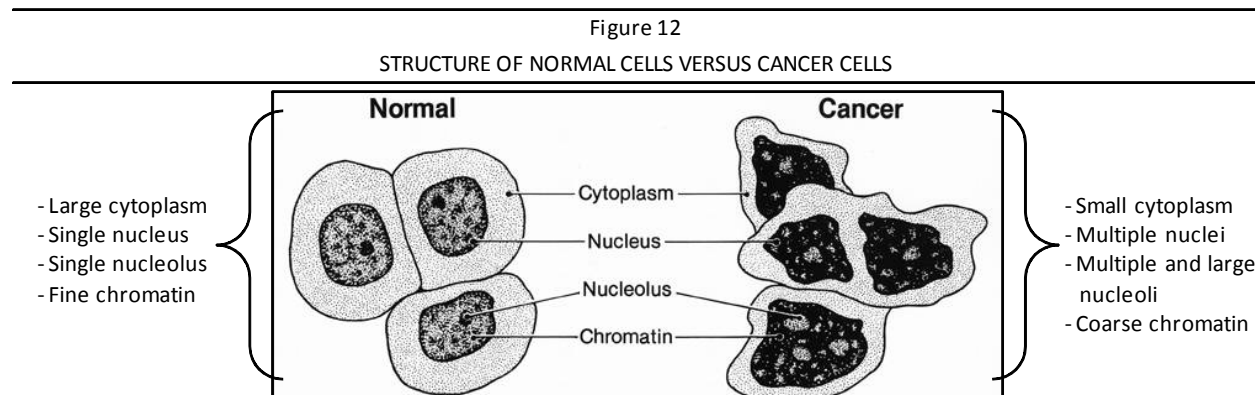
MetaSite™ Breast

MetaStat's near-term product opportunity is MetaSite *Breast*, a diagnostic test designed to predict the likelihood of cancer spreading through the bloodstream to other organs in the body—also called systemic or hematogenous metastasis—in early stage breast cancer. This spread, and the resulting growth of breast cancer tumors in new organs, is responsible for up to 90% of breast cancer fatalities. Currently in a pivotal 500-patient trial (as summarized on pages 31-32), MetaStat expects its MetaSite *Breast* diagnostic test could begin pilot marketing as early as the second half of 2013.

Diagnosis and Monitoring of Metastatic Breast Cancer

While earlier detection and improved treatments have led to lower death rates over the past two decades, breast cancer could be linked to 40,000 deaths during 2012 in the U.S. alone. Physicians currently use various prognostic and predictive factors to diagnose and evaluate patients' risk of cancer progression and metastasis. Professional medical organizations, such as the College of American Pathologists (CAP), have identified a number of factors that are used to help guide physicians when evaluating breast cancer patients, including tumor grade (the degree to which the tumor cells under the microscope look different than normal breast tissue), tumor size, lymph node involvement (number of nodes), hormone status (estrogen/progesterone), **HER2/neu** status, and patient age.

For epithelial solid tumor cancers, such as breast cancer, a sample of tumor tissue is removed by core biopsy, lumpectomy, or mastectomy, and then evaluated by a pathologist under the microscope. In general, the less the breast tumor resembles normal breast tissue, the more aggressive the cancer may be. Figure 12 illustrates potential differences in normal cells versus cancer cells.



Source: National Cancer Institute.

Staining techniques may also be employed by pathologists to identify receptor sites (locations on the cell surface where molecules can interact with cellular components) for various hormones that help some types of cancer cells grow, such as estrogen or HER2/neu (breast cancer). Approximately 20% of breast cancers produce excess HER2 due to a gene mutation, frequently resulting in a more aggressive cancer (Source: the Mayo Foundation for Medical Education and Research).

Currently, the American Joint Committee on Cancer (AJCC) guidelines for assessing tumor stage uses the TNM system, where "T" stands for tumor size and relationship to adjacent anatomic structures; "N" represents lymph node status; and "M" signifies whether or not distant spread is detected using biopsy or imaging techniques.

Room for Enhanced Prognostic Tools

At present, physicians rely primarily on tumor grade and stage to estimate the likelihood of metastasis, but are well aware of the shortcomings in this approach. Given their experience working with cancer patients, some physicians report that this method results in improper classification for some patients. Patients that are improperly classified as "high risk" may be exposed to months of aggressive chemotherapy and radiation treatments that

cause severe side effects (as summarized in Figure 13) and can dramatically impact quality of life. Similarly, patients incorrectly classified as “low risk” may not receive timely and necessary treatment. As the efficacy of treatment varies significantly across cancer populations, the cost of the therapy and the physical and mental burdens associated with treatment may not always be justified.

Figure 13
A SELECTION OF POTENTIAL SIDE EFFECTS OF CHEMOTHERAPY AND RADIATION THERAPY

Chemotherapy Side Effects			Radiation Therapy Side Effects
▪ anemia	▪ infection	▪ neuropathy	▪ skin reactions
▪ bone loss/osteoporosis	▪ memory loss	▪ taste and smell changes	▪ armpit discomfort
▪ diarrhea	▪ menopausal symptoms	▪ vaginal dryness	▪ chest pain
▪ fatigue	▪ mouth and throat sores	▪ vision/eye problems	▪ fatigue
▪ fertility issues	▪ nail changes	▪ vomiting	▪ heart problems
▪ hair changes	▪ nausea	▪ weight changes	▪ lowered white blood cell counts
▪ heart problems			▪ lung problems

Source: Breastcancer.org (<http://www.breastcancer.org>).

One prognostic tool currently available for breast cancer is Genomic Health’s Oncotype DX® Breast Cancer Assay, which evaluates 21 genes to predict the likelihood of a patient benefitting from chemotherapy or suffering from cancer recurrence in early stage breast cancer. Oncotype DX assigns a numerical value to the risk of recurrence and the likelihood that the patient will benefit from chemotherapy in addition to hormonal therapy. Some physicians argue that Oncotype DX does not add to data collected by routine immunohistochemistry—a laboratory test performed on tumor tissue to detect the amount of a specific genetic protein in the cancer calls—and that the confidence intervals for predicting outcome for an individual patient are broad (Source: <http://www.onclive.com>, May 4, 2011). Regardless, since its launch in 2004, Oncotype DX has been used to evaluate over 275,000 patients (Source: Genomic Health’s Investor Presentation, May 15, 2012). The test is reimbursed by many insurance companies, a contributing factor in its adoption. After achieving sales of over \$174 million in 2010, the Oncotype DX Breast Cancer Assay could reach \$300 million in revenues by 2015 (Sources: Seeking Alpha, March 13, 2012, and BCC Research, November 2010).

To MetaStat’s knowledge, unlike MetaSite *Breast*, the Oncotype DX algorithm is not mechanism based. Rather, it is a mathematical algorithm that relies heavily on proliferation markers and hormone receptor and HER2 status. In contrast, MetaSite *Breast* is mechanism based, which the Company believes could better predict a breast cancer patient’s prognosis.

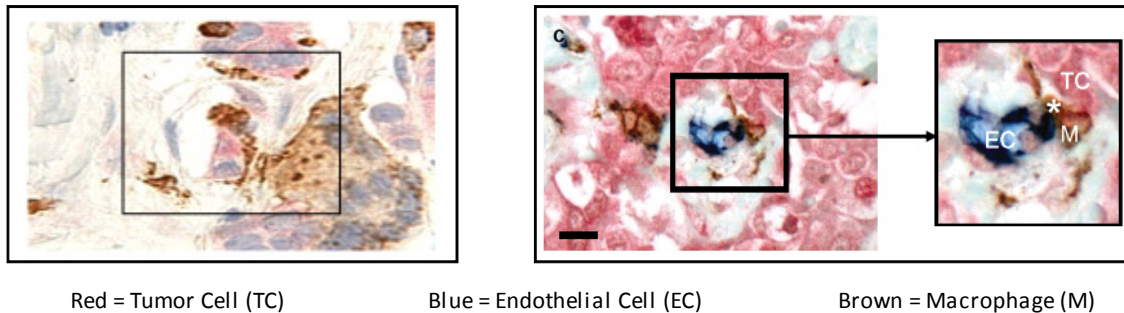
MetaStat’s technology focuses on identifying markers that can predict the risk of cancer advancing based on the mechanisms involved in cancer development and metastasis. Historically, cancer cells have entered the blood vessels via unknown means. The research supporting the Company’s technology has sought to identify structural and behavioral mechanisms that allow cancer cells to move and how this information can be used in prognosis. To MetaStat’s knowledge, its technology is the only technique at present that focuses on mechanistic markers.

The MetaSite *Breast* Test

Through the research summarized on pages 19-26, a collaboration of scientists from MIT, the Albert Einstein College of Medicine, and Weill Cornell Medical School discovered the actual site of metastasis or “MetaSite” that allows metastatic cells to enter into the bloodstream and spread to other areas of the body, and reasoned that the quantity of MetaSites correlated to the probability of distant site metastases. Subsequently, the team of researchers developed the MetaSite *Breast* clinical laboratory test to predict whether a breast cancer patient’s tumor will spread to other parts of the body. It employs conventional immunostaining techniques that allow the pathologist to clearly see and count the three-cell MetaSite structures in tumor tissue samples (as shown in Figure 14 [page 29]). The stain contains antibodies to the three cell types found in the MetaSite. The test result is designed to provide physicians and patients with critical information on metastatic potential that is highly specific to the individual tumor. The Company intends to provide both a quantitative score based on the number of MetaSites as well as an accompanying interpretation of what the score indicates in terms of the risk of developing metastasis and classification of the patient into a low, medium, or high-risk group.

Figure 14

METASITES VISUALIZED AFTER METASITE *BREAST'S* TRIPLE IMMUNOHISTOCHEMICAL STAIN



Sources: MetaStat, Inc. and *Clinical Cancer Research* 2009; 15(7).

MetaStat believes that its MetaSite *Breast* test could be the first product to help breast cancer patients and their physicians make informed decisions on whether or not to proceed with aggressive therapy by providing a prediction of the risk that their cancer will spread.

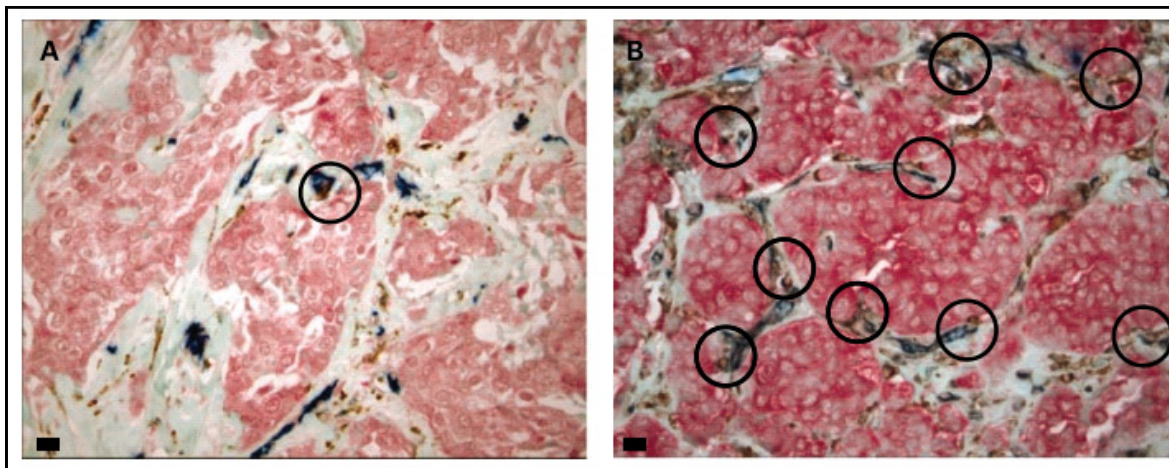
Favorable Clinical Data to Date

To date, MetaSite *Breast* has been validated in two human clinical studies. In one study, MetaSite *Breast* was used on 30 paraffin-embedded samples from primary breast cancer patients who eventually developed metastatic breast cancer and 30 samples from breast cancer patients without metastatic disease. The case-control study was designed to compare breast cancer subjects who suffered metastatic disease with patients who did not develop metastases but were otherwise similar based on currently used prognostic criteria (the control group). All patients were followed for a minimum of five years. Without knowing which tissue sample belonged to which group, pathologists applied the triple immunohistochemical stain to each sample to identify MetaSites or potential tumor microenvironments of metastasis (TMEMs). The number of MetaSites (TMEMs) were counted for each patient, and increased density of TMEMs correlated significantly with metastasis.

Figure 15 illustrates a case-control comparison of tumors with similar histological grade stained for TMEM. The non-metastatic patient had low TMEM density (A, left side) while the patient who later developed metastases showed significantly more MetaSites (B, right side). The density of any of three MetaSite components individually—a carcinoma cell, macrophage, or endothelial cell—was not sufficient to predict the clinical outcome.

Figure 15

COMPARISON OF TMEM COUNTS* IN A METASTATIC AND A NON-METASTATIC TUMOR WITH SIMILAR HISTOLOGICAL GRADES



* Each circle depicts one TMEM (or three-cell "MetaSite") after triple immunostaining. Original magnification, 400; bar, 20 μ m; circles, 60 μ m in diameter.

Source: *Clinical Cancer Research* 2009;15(7).

The researchers concluded that TMEM density was significantly correlated with hematogenous metastases, and may be useful as a prognostic marker for patients with breast cancer. The number of MetaSites varied widely from 12 (low risk) to over 240 (high risk). Data from the study showed that the patient group that eventually developed metastasis had higher MetaSite or TMEM density (median 105) versus the control group (median 50), as shown in Figure 16.

Figure 16

TMEM DENSITY IN THE NON-METASTATIC AND METASTATIC PATIENT GROUPS

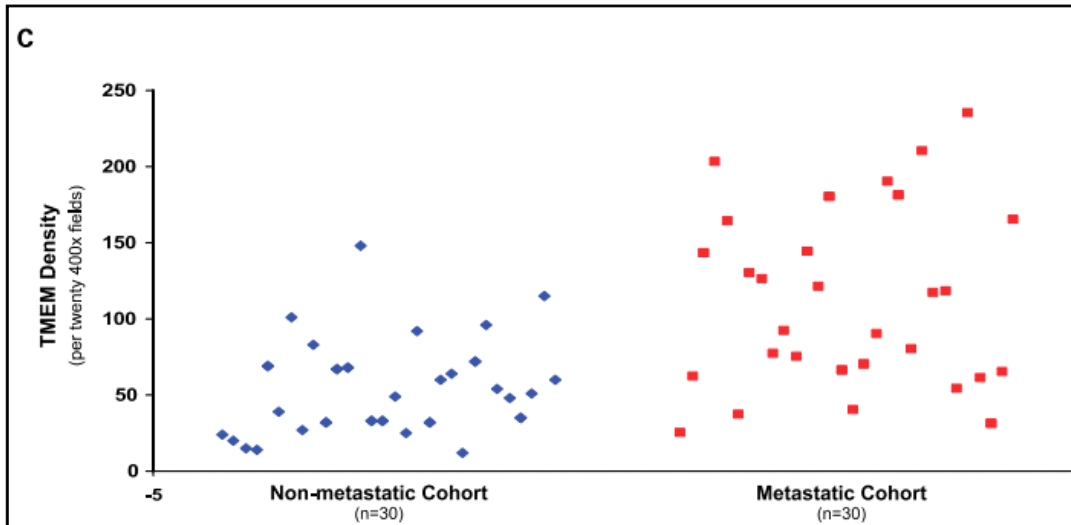


Table 2. Case-control study results

(A) TMEM density

	Metastatic cohort (n = 30)	Nonmetastatic cohort (n = 30)	P
Median (5th percentile, 95th percentile)	105 (28.3, 221)	50 (13.1, 130)	0.00006

(B) Increase in risk of metastasis per 10-unit increase in TMEM

Adjusted for	Odds ratio (95% confidence interval)
(Unadjusted)	1.9 (1.1-3.4)
Age at diagnosis	1.9 (1.1-3.4)
Tumor grade	1.9 (1.1-3.4)
Tumor size	1.9 (1.1-3.3)
Lymphovascular invasion	1.5 (0.95-2.3)
Lymph node metastasis	1.9 (1.0-3.6)
Estrogen receptor status	2.0 (1.1-3.7)
Progesterone receptor status	1.9 (1.0-3.6)
HER-2/neu status	2.2 (1.1-4.7)

NOTE: TMEM density was significantly higher in the group of patients who developed distant metastasis compared with those with localized breast cancer (A). Additionally, for every 10-unit increase in TMEM, the odds of metastasis almost doubled (B). This estimate was robust to adjustment (separately) for the commonly used prognostic criteria listed in the table, including tumor grade, emphasizing that TMEM is not a surrogate for grade and may be a useful new independent prognostic factor.

Source: *Clinical Cancer Research* 2009;15(7).

For every 10 TMEMs, the odds of systemic metastasis nearly doubled (with a 95% confidence interval). Importantly, the ability of TMEM to predict distant metastasis was independent of conventional prognostic indicators, including tumor size, grade, lymph node metastasis, lymphovascular invasion, or hormone receptor status. In 2009, the study was published in *Clinical Cancer Research* and entitled “Tumor Microenvironment of Metastasis in Human Breast Carcinoma: A Potential Prognostic Marker Linked to Hematogenous Dissemination.” Three of the study’s authors now reside on MetaStat’s Scientific Advisory Board, including Dr. John Condeelis (chairman), Dr. Thomas Rohan, and Dr. Frank Gertler. As well, Dr. Joan Jones is a member of the Company’s Clinical Advisory Board.

MetaSite Breast Provides Key Information for Breast Cancer Prognosis

The Company has also evaluated the MetaSite *Breast* test against Genomic Health's Oncotype DX® Breast Cancer Assay. In a study of 44 breast cancer patients, the Oncotype DX Recurrence Score was compared to the MetaSite count. Data from the study revealed a correlation coefficient of 0.19, indicating that the two tests are largely independent. MetaStat believes that, if repeated in a larger study, the data could indicate that MetaSite *Breast* supplies valuable information beyond the Oncotype DX test and holds the potential to become an important element in the clinical care and stratification of breast cancer patients.

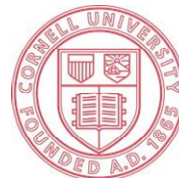
In both trials (MetaSite *Breast* independently and in comparison to Oncotype DX), MetaStat divided participants into three cohorts based on the MetaSite count: low, medium, and high risk. The Company found that patient samples classified as high-risk were 22 times more likely to experience metastasis than the low-risk group. Oncotype DX also separates patients into three risk-level groups; however, with a group average of a 31% risk of recurrence, the high-risk group is believed to be only 4.5 times more likely to recur than the low-risk group (7%).

Ongoing Large-Population Validation Study in Breast Cancer Patients

MetaStat is currently conducting a study of 500 patients with two sponsored research partners: the Albert Einstein College of Medicine and Weill Cornell Medical College (Figure 17). The retrospective study, in which patients have been followed for a minimum of five years, is being performed on already-collected human cancer tissue samples with accompanying patient medical histories. When a tumor is excised at a major cancer research center, sections of the tumor are often preserved and archived to support ongoing and future cancer research. Rather than testing a patient and performing a prospective five-year follow-up, MetaStat is able to access these archived cancer tissues with accompanying medical records but without personal information (negating the need for informed consent). The tissue samples for MetaStat's study were provided by Kaiser Permanente, a nonprofit health plan provider.

Figure 17

SPONSORED RESEARCH PARTNERS FOR THE ONGOING LARGE POPULATION VALIDATION STUDY



Cornell University

Source: MetaStat, Inc.

The Company has identified two main objectives for the study:

- (1) to further study the relationship between TMEM count at initial diagnosis of invasive ductal carcinoma (the most common type of breast cancer) and a patient's risk of systemic metastasis; and
- (2) to identify a cut-point for stratifying patients into low-, medium-, and high-risk groups (based on TMEM count) based on the likelihood of developing systemic metastasis and to determine the cut-point's sensitivity and specificity.

The Company is using samples from 250 metastatic breast cancer patients and 250 non-metastatic individuals and pairing them as closely as possible based on tumor size, grade, lymph node involvement, and hormone receptor status. MetaStat can then perform the MetaSite *Breast* test on the tissues, and determine the TMEM count and density. Once the data is collected, the MetaSite density can be compared to the known outcome from the medical records—the equivalent of five-year follow-up data acquired in significantly less time and lower cost than performing a prospective human trial. This technique has been utilized for the validation of a number of products on the market today, including Oncotype DX.

The data collected from the study is expected to be used to create a scoring system for the MetaSite *Breast* test. Depending on the quantity and density of MetaSites in a sample, the patient is given a Metastasis Score that falls within the low-, medium-, or high-risk groups for systemic metastasis. The Company intends to provide an accompanying interpretation of what the score indicates in terms of the risk of developing metastasis and classification of the patient into a low, medium, or high-risk group. Physicians and patients can use the information to make more informed treatment decisions.

MetaStat anticipates that results from this trial could be available in the first half of 2013. If the data collected from this study demonstrates a similar predictive ability to the previous 44- and 60-patient studies, the Company could begin pilot marketing the MetaSite *Breast* test as early as the second half of 2013.

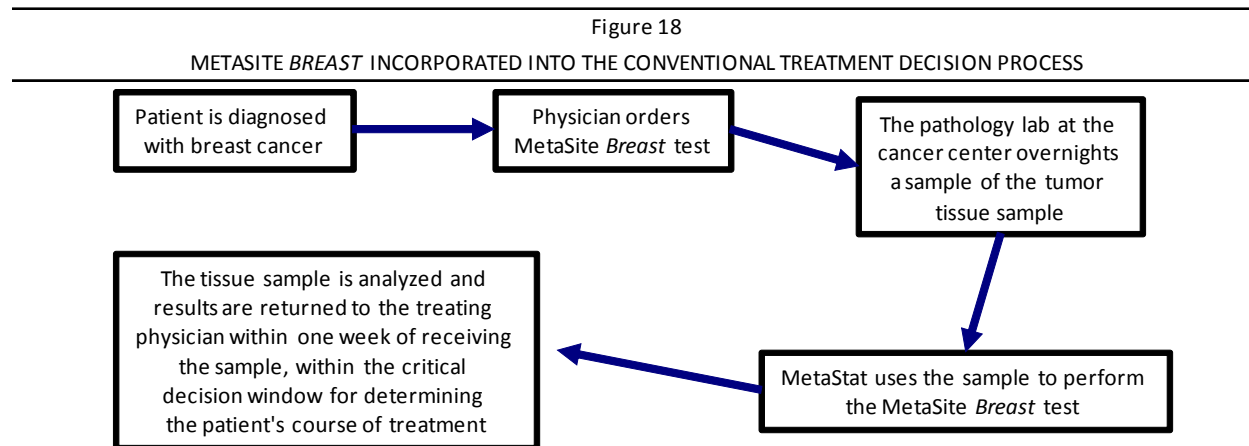
Subsequent Comparison to Oncotype DX

Once MetaStat obtains data from the above study, it expects to gain access to tissue samples that have been scored with Oncotype DX in order to perform a direct comparison of the two tests. The Company, after review of information and data available on the Genomic Health, Inc. website, estimates that the gene signature of Oncotype DX is approximately 60% related to cell proliferation, 38% response to hormones, and 2% to motility and degradation of the extracellular matrix, which varies greatly from the MetaSite *Breast* test. As a result, MetaStat anticipates that its test may not correlate with Oncotype DX results, potentially providing information to physicians that could complement or potentially compete against Genomic Health's recurrence score.

Dr. Gertler, one of the co-developers of MetaStat's technology and a biology professor at MIT, has stated that the MetaSite *Breast* test may offer a more powerful predictive value than currently used assays in clinics, while only requiring pathologists to analyze histological samples or tissue samples (Source: <http://youtu.be/4fHywHv-l24>).

MetaStat's Marketing and Commercialization Strategy for MetaSite *Breast*

MetaStat expects to establish a clinical reference laboratory that can be responsible for receiving and analyzing all tumor samples collected using the MetaSite *Breast* test and returning a Metastasis Score report to physicians within a week of receiving the sample for analysis. Figure 18 summarizes how MetaSite *Breast* can be incorporated into the traditional treatment decision process without requiring physicians to perform additional procedures on the patient or to purchase any new equipment.



Source: MetaStat, Inc.

An advantage of MetaSite *Breast* is that it employs widely available immunohistochemical tissue staining techniques and allows operators to view different cell types on a single slide using different dye colors. Initially, the Company expects one Leica BOND-III immunohistochemical staining cabinet (shown in Figure 19) to be sufficient to process MetaSite *Breast* tests. As such, MetaStat believes that this approach may be more cost effective than marketed products that use genomic-based techniques.

Figure 19

INITIAL LABORATORY EQUIPMENT AND PERSONNEL NECESSARY FOR METASITE *BREAST* TEST ANALYSIS

Initially, MetaStat can support processing of the the MetaSite *Breast* test with one Leica BOND-III immunohistochemical staining cabinet.



Sources: Leica Microsystems Inc. and MetaStat, Inc.

Initially, the Company expects the laboratory to be able to support up to 1,000 tests per quarter, with the potential to expand capacity to 15,000 tests quarterly by the end of 2015. To maintain low costs of production, the Company plans to hire one or more contract manufacturers to produce, package, and ship the immunohistochemicals necessary for the MetaSite *Breast* test.

The Company has identified several factors that may drive adoption of the MetaSite *Breast* test following the completion of the 500-patient study, including those shown in Figure 20.

Figure 20

KEY FACTORS THAT COULD DRIVE ADOPTION OF THE METASITE *BREAST* TEST

- Acceptance of the test's clinical benefits by healthcare providers
- Demonstration of the cost-effectiveness of using the test
- Reimbursement by third-party and government payors, including Medicare and Medicaid
- Expansion of MetaStat's sales force and increased marketing efforts
- Publication of peer-reviewed articles and/or studies
- Clinical presentations at major symposia and conferences, such as the American Society of Clinical Oncology (ASCO)
- Inclusion of the MetaSite *Breast* in clinical practice guidelines

Source: MetaStat, Inc.

Pilot Marketing Program

After completing an internal review of data from the ongoing validation study, MetaStat plans to commence pilot marketing to opinion leaders at select cancer centers in select U.S. markets, which will likely be supported by a small direct sales force. The Company's management team and Scientific Advisory Board have pre-existing relationships with the cancer centers listed below, which represent potential targets for the pilot marketing program.

- New York-Presbyterian/Weill Cornell Medical Center
- Montefiore Medical Center, the University Hospital for the Albert Einstein College of Medicine
- Memorial Sloan-Kettering Cancer Center, which handles a large number of breast cancer cases
- M.D. Anderson Cancer Center, the largest freestanding cancer center in the world (Source: www.mdanderson.org)

MetaStat aims to grow these relationships and nurture new relationships with other cancer centers to spread awareness of its novel diagnostic for breast cancer. To date, the Company has showcased its technology at major cancer centers, such as the M.D. Anderson Cancer Center and Montefiore Medical Center. Based on discussions with heads of the breast medical oncology departments at these organizations, the Company has reported that its MetaSite *Breast* test could expand the cancer diagnostics market while helping payors lower costs through customized cancer therapy.

Comprehensive Marketing Strategy

Pending final results from its study, the Company expects to launch a full marketing program in 2014 targeting the oncology community, including medical and surgical oncologists. This program will likely be supported by a sales team experienced in clinical oncology selling and marketing to biopharmaceutical, pharmaceutical, and specialty reference laboratory companies. The sales team's primary goals are expected to include spreading awareness of the test and its clinical and economic benefits to physicians, laboratory personnel, and other healthcare professionals and working closely with national and regional patient advocacy organizations for breast cancer care. MetaStat also plans to develop a website with clinical information for healthcare professionals and educational materials for breast cancer patients.

MetaStat anticipates that its marketing agenda can be augmented by publishing its clinical data in a peer-reviewed scientific/medical journal and presenting at industry gatherings, such as the American Society of Clinical Oncology (ASCO) Annual Meeting and the San Antonio Breast Cancer Symposium, which MetaStat believes could help drive demand. The Company aims for the MetaSite *Breast* test to be integrated into ASCO's guidelines for the use of breast cancer tumor markers, which outline appropriate methods of treatment and care, and for the Metastasis Score to become part of a standard pathologist's report, which presently includes data on tumor size, grade, lymph node involvement, hormone status, and recurrence score (provided by the Oncotype DX test).

As well, the Company plans to complete additional clinical studies to further demonstrate the effectiveness and economic benefit of the MetaSite *Breast* test, which MetaStat believes could help gain market acceptance, increase market penetration, and obtain favorable reimbursement coverage from third-party payors.

Potentially Reducing the Costs of Cancer Treatment

MetaStat may be able to reduce cancer treatment costs by providing physicians/patients with critical information before the course of action for treatment is finalized. When metastasis risks are not properly assessed, patients may undergo toxic and costly chemotherapy regimens that were unnecessary or, conversely, may receive insufficient treatment, allowing the cancer to progress. An eight-week regimen of chemotherapy can cost as much as \$30,000 (Source: Livestrong.com, "The Average Cost for Cancer Chemotherapy Treatment," March 31, 2011). As well, if a high-risk breast cancer patient is misclassified as low risk, the individual may miss the opportunity to treat the cancer in the early stages, when it is most treatable, potentially necessitating future treatment that may be more costly and may not yield the most beneficial results, if the cancer spreads.

In addition, the Company estimates its list price of \$2,595 for MetaSite *Breast* is significantly less than existing diagnostic products for breast cancer, including Oncotype DX, which has a list price of \$4,175 (Source: Genomic Health's *Oncotype DX® DCIS Clinical Compendium*, February 10, 2012).

Third-Party Reimbursement Strategy

MetaStat aims to follow the strategy used by Genomic Health for obtaining insurance coverage, which resulted in Genomic Health entering into reimbursement agreements with both regional and larger national payors shortly after publishing its validation trial results in 2004. This strategy will likely entail expending resources to educate payors, such as Kaiser Permanente, Aetna (AET-NYSE), and United Healthcare (among others), about the test's performance, clinical utility and effectiveness, publication in peer-reviewed journals and consistent study outcomes, patient and physician demand, and economic benefits. The Company must also work with the Centers for Medicare and Medicaid Services (CMS) for reimbursement by government payors, Medicare and Medicaid.

In addition to commercial third-party and government payors, MetaStat may also earn revenues from patient self-pay and in some cases from hospitals or referring laboratories that, in turn, may bill third-party payors.

Market Opportunities for MetaSite *Breast*

Breast cancer is one of the most commonly diagnosed cancers for females, accounting for nearly one in three cancers diagnosed in U.S. women (Source: the American Cancer Society's *Breast Cancer Facts & Figures, 2011-2012*). In 2011, an estimated 230,480 women were diagnosed with invasive breast cancer in the U.S., and nearly 40,000 females died as a result of the disease, as shown in Figure 21. In 2008, the National Cancer Institute estimated that approximately 2.6 million women were living with a breast cancer diagnosis in the U.S.

Figure 21
ESTIMATED NEW FEMALE BREAST CANCER CASES AND DEATHS BY AGE, U.S., 2011*

Age	In Situ Cases	Invasive Cases	Deaths
Under 40	1,780	11,330	1,160
Under 50	14,240	50,430	5,240
50-64	23,360	81,970	11,620
65+	20,050	98,080	22,660
All Ages	57,650	230,480	39,520

* Rounded to the nearest 10.

Note: Total estimated cases are based on 1995-2007 incidence rates from 46 states as reported by the North American Association for Central Cancer Registries. Total estimated deaths are based on data from U.S. Mortality Data, 1969-2007, National Center for Health Statistics, Centers for Disease Control and Prevention.

Source: American Cancer Society, *Surveillance Research, 2011*.

Based on data from the 60-patient trial, which demonstrated that metastatic outcome was independent of clinicopathologic characteristics including age, tumor grade, tumor size, lymph node involvement, and hormone status, MetaStat believes that the MetaSite *Breast* test can be applicable to all breast cancer patients, regardless of hormone receptor status or lymphovascular invasion. As such, the test could be useful for patients diagnosed with triple-negative breast cancer (cancer that lacks receptors for estrogen, progesterone, and HER2/neu), which does not respond to hormonal therapy or therapies that target HER2 receptors and is often an aggressive cancer.

MenaCalc™ Diagnostic Platform

The MenaCalc™ technology platform is based on research conducted by the Licensors, which have found that patients' potential for cancer metastasis could likely be determined by measuring their relative amounts of Mena isoforms, offering clinicians a more complete picture upon which to base a patient's treatment strategy. Further, a patient's Mena isoform profile could be documented over time, which could be used to identify trends and detect stability or progression of the disease over time, as well as to detect the efficacy of various therapies in real time.

As a result of preclinical research and data from ongoing clinical studies, MetaStat is currently developing three products based on the MenaCalc diagnostic platform:

- MenaCalc *Breast*;
- MenaCalc *Lung*; and
- MenaCalc *Prostate*.

The Company is pursuing trademark protection for each of these names. Clinical studies have taken place at MIT, Cornell, and Yale University, with two trials recently completed at Yale. The results of one of these trials have been published in *Breast Cancer Research* during 2012 in an article, entitled "Quantitative Assessment of Invasive Mena Isoforms (MenaCalc) as an Independent Prognostic Marker in Breast Cancer" (Source: Agarwal et al., *Breast Cancer Research* 2012; 14[5]: R124).

MenaCalc *Breast*

MenaCalc *Breast* is an individualized tissue-based test that can be performed on disassociated, discontinuous cells obtained by a needle biopsy of breast cancer tissue (in a standard biopsy procedure known as "**fine needle aspiration**"). After extraction from the patient, the cells are evaluated for the presence and ratio of the noninvasive Mena 11a isoform to the invasive Mena^{INV} isoform.

As published in *Clinical & Experimental Metastasis* in 2011 in an article entitled, "Mena invasive (Mena^{INV}) and Mena11a isoforms play distinct roles in breast cancer cell cohesion and association with TMEM," and detailed on pages 24-26 of this Executive Informational Overview® (EIO), Mena^{INV} is associated with greater tumor metastasis than noninvasive Mena (Source: Roussos et al., *Clinical & Experimental Metastasis* 28(6): 515-27). Researchers have found that Mena occurs differently in invasive tumor cells versus "non-motile resident" (i.e., noninvasive) tumor cells, whereby invasive tumor cells express relatively higher levels of Mena^{INV} and lower levels of the Mena 11a isoform, and noninvasive tumor cells express relatively lower levels of Mena^{INV} but express relatively higher levels of Mena 11a.

Using the MenaCalc diagnostic platform, MetaStat can determine each patient's individual expression levels of the isoforms of the Mena protein in cancer tissue. The relationship between Mena 11a and Mena^{INV} is used to compute a "MenaCalc *Breast* Metastasis Score," which may predict a breast cancer patient's individual metastatic profile (i.e., determining whose cancer is likely to continue to spread and whose may stay localized) as early on in disease progression as possible. Because it is designed to be effective on disassociated cells, the MenaCalc *Breast* test may eventually represent a valuable tool for determining prognosis before the patient undergoes surgery to remove the tumor(s).

Trial at Albert Einstein College of Medicine and the Yale University School of Medicine

MetaStat reports that research to date has illustrated a correlation between the MenaCalc *Breast* Metastasis Score and the MetaSite *Breast* Metastasis Score, which is being confirmed in a trial at the Yale University School of Medicine. The Company has conducted an 800-patient study at Yale confirming the predictive value of the MenaCalc *Breast* Metastasis Scores. Data from this trial was published in *Breast Cancer Research* during 2012 in an

article, entitled “Quantitative Assessment of Invasive Mena Isoforms (MenaCalc) as an Independent Prognostic Marker in Breast Cancer” (Source: Agarwal et al., *Breast Cancer Research* 2012; 14[5]: R124).

Following the completion of the 800-patient confirmatory trial, MetaStat anticipates initiating a large-scale, 550- to 1,000-patient validation study of the MenaCalc *Breast* test.

MenaCalc *Lung*, MenaCalc *Prostate*, and Additional Indications

In addition to MenaCalc *Breast*, MetaStat believes the MenaCalc technology may be suitable as a new diagnostic tool for an array of cancers. As detailed on pages 19-26, the Mena protein is thought to be a key factor contributing to the progression of metastasis in multiple solid tumors, potentially including pancreas, prostate, colon, brain, liver, lung, head, and neck tumors as well as breast cancer. As these cancers represent many of the world’s most common tumor types, diagnostic and prognostic tests based on the MenaCalc platform may ultimately address millions of patients globally.

To this effect, MetaStat has already begun evaluating MenaCalc’s efficacy in lung and prostate cancers. Data collected to date using MenaCalc in lung adenocarcinoma demonstrates high predictive accuracy in distant metastasis. In early 2011, the Company completed a pilot study at MIT that produced promising preliminary data supporting the ability of a MenaCalc *Prostate* test for predicting prostate cancer metastasis. Consequently, MetaStat now plans to conduct a larger, confirmatory trial for the MenaCalc *Prostate* product candidate. The development of a prognostic test, such as MetaStat’s for prostate cancer, could be particularly beneficial for patients and physicians alike, as it would allow patients to make an informed decision regarding treatment based on the knowledge of whether or not their tumor will metastasize. Prostate tumors are by nature slow growing, and many men die of old age before they are affected by their prostate cancer (Source: National Cancer Institute). By knowing their risk of the tumor spreading, prostate cancer patients can decide between active surveillance and surgery or radiation therapy, thereby allowing patients with favorable metastasis profiles to avoid the risks associated with high-impact cancer treatments.

The Company has also completed a 70-patient study at Yale, designed to evaluate the ability of MenaCalc *Lung* to predict metastasis of lung adenocarcinomas. The study confirms the ability of MenaCalc *Lung* to predict survival. MetaStat plans to perform a larger, confirmatory trial for MenaCalc *Lung*.

In the future, Dr. Gertler and fellow researchers may also pursue development of a test to measure Mena using only a blood sample, in order for it to be performed well before a tumor is biopsied or excised (Source: <http://youtu.be/4fHywHv-l24>). The Company intends to pursue the development of a Mena blood test in the future as funding permits.

MenaBloc™ Cancer Metastasis Therapeutic

Going forward, MetaStat's pipeline may further include a therapeutic molecule designed to inhibit the Mena protein. Based on research conducted by the Licensors, MetaStat intends to begin screening candidate molecules in 2013 as part of its MenaBloc™ therapeutic platform.

Preclinical Research Supporting the Development of a Mena-inhibitor Therapeutic

Believing that the Mena protein may have a role in the metastasis (or spread) of cancer beyond the initial tumor site, scientists from the Albert Einstein College, MIT, Cornell, and IFO-Regina created a mouse type that was unable to produce this protein. These mice are known as "Mena null" mice. Once developed, researchers cross bred the Mena null mice with PyMT mice, which are known to be genetically predisposed to highly metastatic breast cancer. Thus, the resulting mice were afflicted with metastatic breast cancer but did not have the Mena protein.

The engineered Mena null, PyMT mice described above were then compared to typical PyMT mice, which formed the control group for these studies. Without the Mena null cross-breeding, typical PyMT mice are commonly used as a model for human breast cancer tumors. These mice are predisposed to develop metastatic breast cancer that goes through distinct stages of tumor progression and metastasis comparable to the progression of human breast disease.

Result Highlights

Importantly, researchers found that while both groups of mice developed breast cancer tumors, only the control mice showed metastatic tumors. Due to the rapid spread of disease in the control mice, all of these subjects were killed by their tumors. In contrast, cancer in the Mena null, PyMT mice remained localized and these subjects showed a significant survival advantage. Most Mena null, PyMT mice were able to die of old age.

Figure 22 (page 39) illustrates a selection of key data from this research, noting that mice were considered "not moribund"—mice that have not yet developed tumors or that have small tumors that have not immobilized them—until their death. Mice with excessive tumor burden causing illness or immobilization were euthanized.

For a greater explanation of trial methods and conclusions, please refer to "Mena deficiency delays tumor progression and decreases metastasis in polyoma middle-T transgenic mouse mammary tumors," as published in 2010 in *Breast Cancer Research* (Source: <http://breast-cancer-research.com/content/12/6/R101/>).

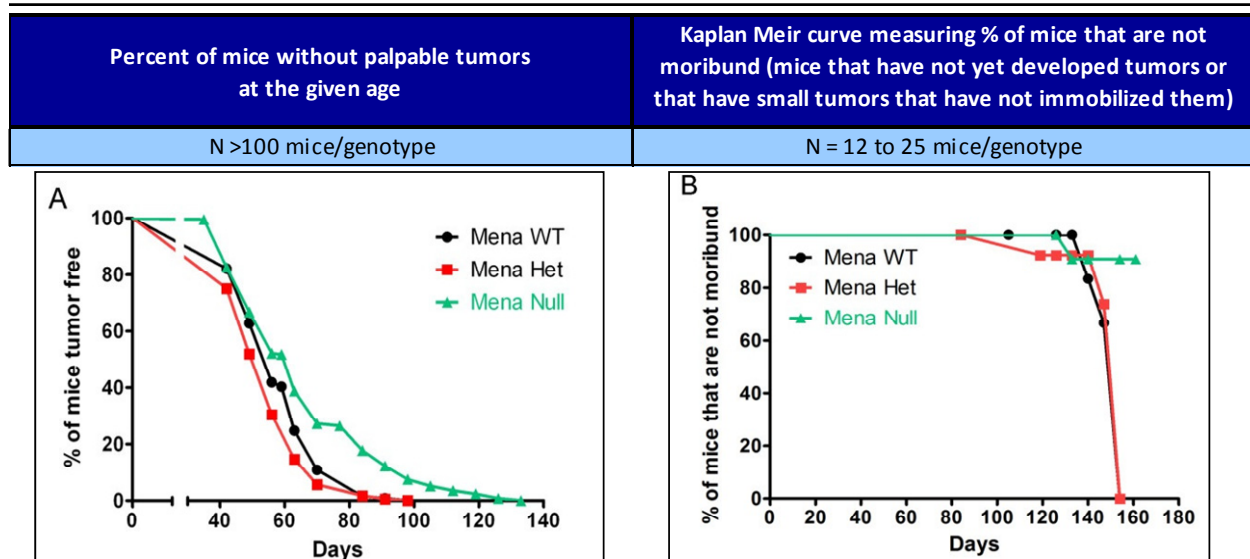
Product Development

As expected, the discovery of a link between the Mena protein and tumor metastasis could lead to the development of new cancer treatments that block the Mena protein in humans in order to slow or stop the spread of patients' breast cancer. Localized disease is considerably easier to treat through surgery and other existing methods, and is consequently associated with higher survival rates than advanced, metastatic disease.

To this end, MetaStat has commenced the design and development of new drug treatments targeted at disabling the action of the Mena protein. The next step in product development on this front is to conduct high-throughput screening of potential molecules that could be used to inhibit Mena. MetaStat intends to sponsor such screening in the coming months, followed by the development of this therapeutic platform under the name "MenaBloc." MetaStat is currently seeking trademark protection for MenaBloc.

Figure 22

A DEFICIENCY OF MENA INCREASES PyMT TUMOR LATENCY AND SURVIVAL IN MICE



Mena WT = Wild Type (control group; PyMT mice where mena is unaffected)

Mena Het = Heterozygote (Mena isoforms are reduced in heterozygote mice versus completely eliminated in Mena null mice)

Mena Null = Mice that lack the Mena protein or its isoforms

Source: Roussos et al. Breast Cancer Research 2010 12:R101 <<http://breast-cancer-research.com/content/12/6/R101/>>.

Competition

Competition for MetaStat includes existing diagnostic products as well as new diagnostics that may be introduced over the coming years as the Company completes development of its products. It can be difficult to change existing diagnostic approaches, as they have become routine procedures used by physicians, pathologists, oncologists, laboratories, and others in the medical community. Although MetaStat is focused on driving development and adoption of its tests for use outside the laboratory, the Company will likely also have to address competition from the kits and reagents used by local pathology labs.

Due to the number of companies and academic or government institutions researching new diagnostic techniques and new cancer therapies, MetaStat may compete with a variety of entities for funding, resources, and market share. These include other developers of diagnostic tests as well as companies that focus on gene profiling and gene or protein expression and commercial laboratories that have strong distribution networks for diagnostic tests. MetaStat believes that its technology and scientific expertise represent a significant competitive advantage.

The selection of companies presented in Figure 23 and detailed thereafter is not intended to be an exhaustive collection of MetaStat's possible competition, yet is believed to be representative of the type of competitors that the Company may encounter going forward.

Figure 23
A SELECTION OF POTENTIAL COMPETITORS

Company	Symbol-Exchange	Last Trade (01/03/13)	52-week Range	Avg. Volume (3 months)	Market Cap.
GE Healthcare Ltd. (a GE unit)	GE-NYSE	\$21.10	\$18.02 - \$23.18	42,673,300	\$221.26 B
Genomic Health, Inc.	GHDX-NASDAQ	\$27.96	\$25.25 - \$37.44	251,377	\$859.74 M
Hologic, Inc.	HOLX-NASDAQ	\$20.72	\$16.18 - \$22.16	2,766,410	\$5.53 B
Laboratory Corp. of America Holdings	LH-NYSE	\$87.70	\$81.56 - \$95.30	722,188	\$8.30 B
Myriad Genetics, Inc.	MYGN-NASDAQ	\$25.57	\$17.51 - \$27.00	775,378	\$2.21 B
Novartis AG	NVS-NYSE	\$63.70	\$51.20 - \$64.40	1,497,780	\$154.06 B
Qiagen N.V.	QGEN-NASDAQ	\$18.69	\$14.36 - \$19.41	642,198	\$4.42 B
Quest Diagnostics Inc.	DGX-NYSE	\$58.37	\$53.25 - \$64.87	839,531	\$9.28 B
Response Genetics, Inc.	RGDX-NASDAQ	\$1.41	\$0.70 - \$2.40	35,772	\$46.24 M
Roche Diagnostics Corp. (a Roche unit)	RHHBY-OTC	\$51.23	\$38.63 - \$51.75	450,857	\$173.61 B
Siemens AG	SI-NYSE	\$109.81	\$77.88 - \$111.37	332,797	\$94.03 B
Veridex LLC (a Johnson & Johnson unit)	JNJ-NYSE	\$70.74	\$61.71 - \$72.74	11,550,400	\$196.04 B
Verastem, Inc.	VSTM-NASDAQ	\$9.84	\$6.25 - \$12.24	27,469	\$209.15 M

Sources: MetaStat Inc., Yahoo! Finance, and Crystal Research Associates, LLC.

GE Healthcare Ltd.

www.gehealthcare.com

GE Healthcare is the global healthcare unit of General Electric Co. (GE-NYSE). It specializes in creating diagnostics, treatments, and other services for cardiology, electrophysiology, emergency care, otolaryngology, musculoskeletal, neurology, oncology, orthopedics, pathology, and women's health. The company leverages advanced diagnostic tools with life science research designed to develop targeted therapies that change the course of today's severe diseases, including numerous cancers and cardiovascular/cerebrovascular conditions. Among standard tests (X-rays, digital mammograms, CT scans, and MRIs), GE Healthcare is also active in molecular imaging technologies. Its medical diagnostics research is directed at marketing imaging agents used to highlight organs, tissue, and functions inside the body in order to aid physicians in the early detection, diagnosis, and management of disease. GE

Healthcare also offers imaging solutions for use in preclinical research for drug development and related applications to deliver complete solutions for molecular imaging research. One of the company's digital pathology solutions is Omnyx™, a comprehensive, scalable research tool that entails whole slide scanners and an integrated software platform for pathology research labs. Omnyx™ was developed jointly by GE Healthcare and the University of Pittsburgh Medical Center to bring enterprise-class IT to laboratories.

Genomic Health, Inc.
www.genomichealth.com

Founded in 2000, Genomic Health is a molecular diagnostics firm focused on commercializing solutions for cancer screening. The company's primary product is the *Oncotype DX*® Breast Cancer Assay, which is a test used to examine patients' breast tumor tissue at a molecular level. Its target population is women who have been diagnosed with Stage I or II, node-negative, estrogen receptor-positive (ER+) breast cancer and who will be treated with hormone therapy. To Genomic Health's knowledge, the *Oncotype DX* assay is the only "multi-gene expression" test commercially available today that has been validated by clinical evidence showing that the test can predict the likelihood of chemotherapy benefit as well as recurrence in early-stage breast cancer. The company has studied its assay in more than 4,000 breast cancer patients globally, comprising 14 separate clinical studies. The *Oncotype DX* technology is also commercially available in an assay for ductal carcinoma in situ patients (where the diagnostic test can make individual predictions of patients' 10-year risk of local recurrence or progression to invasive carcinomas), and in an assay for colon cancer. *Oncotype DX* Colon Cancer is designed to measure the likelihood of recurrence in patients with Stage II color cancer following surgery. The company is further evaluating diagnostic and prognostic products for prostate cancer, non-small-cell lung cancer, renal cancer, melanoma, and additional breast and colon cancer targets.

Hologic, Inc.
www.hologic.com

Women's health company, Hologic, has been in operation for nearly 30 years. Its products and services encompass all aspects of women's health, including laboratory diagnostics for breast and cervical cancer screenings, HPV testing, molecular/genetic testing, and cytology preparation, among others. The company states that its 3D breast tomosynthesis system (digital mammography) is one of the industry's most powerful diagnostic tools for early detection of breast cancer. As well, Hologic provides a ThinPrep® Pap test and related imaging system, the Cellient™ fully automated cell block system, and the FDA-approved and CE-marked TLilQ® in vitro diagnostic device for determining a woman's risk of preterm birth. Hologic's enabling platform technology is called Invader® chemistry, which is a DNA probe-based, specific method for detecting single-base pair changes, insertions, deletions, gene copy number, infectious agents, and gene expression. In August 2012, Hologic completed the acquisition of Gen-Probe Inc. (GPRO-NASDAQ), a molecular diagnostics company, for approximately \$3.8 billion. Gen-Probe is now a wholly-owned subsidiary of Hologic. Gen-Probe's TIGRIS, PANTHER, and APTIMA platforms enable extensive STD testing, including chlamydia/gonorrhea, HPV, and Trichomonas.

Laboratory Corp. of America Holdings
www.labcorp.com

Laboratory Corp. of America Holdings ("LabCorp") operates a network of clinical laboratories and specialized Centers of Excellence across the U.S., where the company provides laboratory tests and services. The company estimates that it performs over one million tests on more than 370,000 specimens each day. In addition to administering testing services, LabCorp works to apply advances in medicine and science to laboratory testing, with more than 35 years of experience in serving physicians and patients. Genomic testing is one of LabCorp's primary initiatives. Its laboratories participated in the development of genomic applications using Polymerase Chain Reaction (PCR) technology and LabCorp states that it was the first commercial laboratory to provide PCR technology to healthcare providers. LabCorp's molecular tests help diagnose, treat, and manage applications in infectious disease, oncology, and genetics.

Myriad Genetics, Inc.www.myriad.com

Salt Lake City, Utah-based Myriad Genetics develops and markets molecular diagnostics tests that have helped physicians manage the healthcare of nearly one million patients in multiple indications. Current efforts are directed at expanding internationally and introducing new molecular diagnostic tests for disease states such as diabetes, depression, and rheumatoid arthritis. In June 2012, Myriad Genetics received the 2012 Charles R. Smart Visionary Award from the American Cancer Society. The company's marketed products include BRACAnalysis® (predictive test for hereditary breast and ovarian cancer), COLARIS® (predictive test for hereditary colorectal cancer or hereditary uterine cancer), MELARIS® for hereditary melanoma, PANEXIA® for hereditary pancreatic and related cancers, OnDose™ testing to measure exposure to 5-FU chemotherapy, Prolaris™ for prostate cancer, and many others.

Novartis AGwww.novartisdiagnostics.com

Novartis, through its subsidiaries, engages in the research, development, and marketing of healthcare products worldwide. Its pharmaceuticals division offers prescription medicines in various therapeutic areas, including cardiovascular and metabolism, oncology, neuroscience and ophthalmics, and respiratory conditions. The company's Vaccines and Diagnostics unit markets instruments, assays, and software for screening 25 million blood donations a year as well as over 20 products to fight viral and bacterial diseases. Novartis was founded in 1895 and is headquartered in Basel, Switzerland.

Qiagen N.V.www.qiagen.com

Qiagen markets over 500 sample and assay technologies as well as automated solutions worldwide. The company's products target epigenetics, FFPE sample analysis, gene expression analysis, gene silencing, genotyping, miRNA research, plant research, and protein science. Its diagnostics tools are sold to molecular diagnostics laboratories, academic researchers, pharmaceutical and biotechnology companies, and applied testing customers. Qiagen possesses 35 global locations.

Quest Diagnostics Inc.www.questdiagnostics.com

Quest Diagnostics offers access to testing and services throughout the U.S. and beyond. In addition to these diagnostics services, the company develops and manufactures diagnostic devices, test kits, and reagents. These products are used by physicians, hospitals, blood collection centers, and other clinical laboratories. Products range from molecular testing platforms, such as Simplexa® for infectious diseases, to portable handheld devices for rapid lab-quality screening near the patient. Quest has recently acquired Athena Diagnostics, Celera Corporation (which now comprises a product line in Quest's Diagnostic Products unit), and S.E.D. Medical Laboratories.

Response Genetics, Inc.www.responsegenetics.com

California-based Response Genetics is a CLIA-certified clinical laboratory focused on the development and sale of molecular diagnostic tests for cancer. The company's proprietary tests and panels target lung, colon, gastric cancer, and melanoma, where they are used to analyze gene expression and mutation in order to assist physicians with treatment decisions. In addition to diagnostic testing, Response Genetics generates revenue from the sale of analytical testing services of clinical trial specimens to the pharmaceutical industry. Its clients have included GlaxoSmithKline plc (GSK-NYSE), Roche, and Taiho Pharmaceutical Co., LTD.

Roche Diagnostics Corp.

www.roche.com/diagnostics

Headquartered in Basel, Switzerland, Roche Holdings is a global healthcare company with pharmaceutical and diagnostic products addressing oncology, virology, inflammation, metabolism, the central nervous system, in vitro diagnostics, tissue-based cancer diagnostics, and diabetes, among others. Roche's Diagnostics division offers products and services for all fields of medical testing. Its products range from at-home blood glucose monitoring devices, point-of-care devices, and in vitro tests for cancer screening/monitoring to high-throughput laboratory systems and state-of-the-art instruments for genetic research. The company's hemo FEC® test offers preventive screening for intestinal cancer that can obtain results within 30 seconds. Roche Diagnostics also entails a number of healthcare segments beyond oncology, such as cardiology.

Siemens Healthcare Diagnostics

www.siemens.com/about/en/businesses/healthcare/diagnostics.htm

As part of global conglomerate Siemens AG, Siemens Healthcare Diagnostics performs in vitro diagnostics for healthcare professionals, hospitals, reference laboratories, and physicians' offices. Altogether, the company offers more than 900 tests and serves 30,000 customers across 120 countries.

Veridex LLC

<http://www.veridex.com>

Veridex is a Johnson & Johnson Company (JNJ-NYSE) specializing in providing in vitro diagnostic oncology products targeted to early disease detection and personalized treatment management. One of its primary initiatives is CellSearch®, a Circulating Tumor Cell (CTC) blood test that assesses CTCs to determine prognosis for metastatic breast, colorectal, or prostate cancer. Veridex is headquartered in New Jersey.

Verastem, Inc.

www.verastem.com

With headquarters in Cambridge, Massachusetts, Verastem is focused on the discovery and development of drugs that target and kill cancer stem cells. The company is developing small molecules designed to inhibit signaling pathways that are critical to cancer stem cell survival and proliferation, including focal adhesion kinase (FAK), PI3K/mTOR, and Wnt. In July 2012, Verastem in-licensed exclusive, worldwide commercial rights to VS-6063 (formerly PF-04554878), a FAK inhibitor that completed a Phase I clinical study in advanced solid tumors, from Pfizer Inc. (PFE-NYSE). The company reports that VS-6063 could enter into a Phase II mesothelioma study in 2013. Verastem is also developing an additional FAK inhibitor, VS-4718, for which toxicology studies are ongoing and a Phase I study could initiate in 2013. The company's dual PI3K/mTOR inhibitor, VS-5584, may begin Phase I testing in 2013 as well. In July 2012, Verastem entered into a research collaboration with Eisai Co., Ltd. to discover next-generation small molecule inhibitors of Wnt signaling.

Historical Financial Results

Figures 24, 25, and 26 provide a summary of MetaStat's key historical financial statements: its consolidated Statements of Expenses, Balance Sheets, and Statement of Cash Flows. MetaStat's unaudited condensed financial statements were prepared on a going concern basis.

Figure 24
MetaStat, Inc. and Subsidiary
(A Development Stage Company)
CONSOLIDATED STATEMENTS OF EXPENSES (Unaudited)

	Three Months ended Aug. 31, 2012	Three Months ended Aug. 31, 2011	Six Months ended Aug. 31, 2012	Six Months ended Aug. 31, 2011	Period from Inception (July 22, 2009) to Aug. 31, 2012
OPERATING EXPENSES					
General & administrative	\$ 540,840	\$ 152,895	\$ 873,698	\$ 211,500	\$ 1,781,088
Research & development	277,517	55,000	333,517	413,777	1,357,922
Depreciation	3,081	164	5,413	328	6,684
Warrant Expense	—	—	—	—	149,999
Stock-based compensation	11,075	—	11,075	—	769,910
Total Operating Expenses	832,513	208,059	1,223,703	625,605	4,065,603
OTHER INCOME (EXPENSE)					
Interest Income	116	—	348	—	348
NET LOSS	<u>\$ (832,397)</u>	<u>\$ (208,059)</u>	<u>\$ (1,223,355)</u>	<u>\$ (625,605)</u>	<u>\$ (4,065,255)</u>
 Basic & Diluted Net Loss Per Share	<u>\$ (0.04)</u>	<u>\$ (0.01)</u>	<u>\$ (0.06)</u>	<u>\$ (0.04)</u>	
 Weighted shares outstanding	<u>21,053,335</u>	<u>15,953,767</u>	<u>20,707,357</u>	<u>15,793,974</u>	

Source: MetaStat, Inc.

Figure 25
MetaStat, Inc. and Subsidiary
(A Development Stage Company)
CONSOLIDATED BALANCE SHEETS (Unaudited)

	August 31, 2012	February 29, 2012
ASSETS		
CURRENT ASSETS		
Cash	\$ 970,729	\$ 878,340
Certificate of deposit	250,182	—
Subscription receivable	25,000	865,000
Total Current Assets	1,245,911	1,743,340
PROPERTY AND EQUIPMENT		
EQUIPMENT (net of accumulated depreciation of \$6,684 and \$1,271, respectively)	52,607	19,208
TOTAL ASSETS	<u>\$ 1,298,518</u>	<u>\$ 1,762,548</u>
LIABILITIES AND STOCKHOLDERS' EQUITY		
LIABILITIES		
Accounts payable	\$ 160,109	\$ 291,859
TOTAL LIABILITIES	160,109	291,859
STOCKHOLDERS' EQUITY		
Preferred Stock (50,000,000 shares authorized; no shares issued and outstanding, respectively)	—	—
Common Stock (Common Stock, \$0.0001 par value; 150,000,000 shares authorized; 21,054,422 and 20,074,422 shares issued and outstanding, respectively)	2,106	2,008
Paid-in-capital	5,201,558	4,310,581
Accumulated deficit as a development stage company	(4,065,255)	(2,841,900)
Total Equity	1,138,409	1,470,689
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	<u>\$ 1,298,518</u>	<u>\$ 1,762,548</u>

Source: MetaStat, Inc.

Figure 26
MetaStat, Inc. and Subsidiary
(A Development Stage Company)
CONSOLIDATED STATEMENT OF CASH FLOWS (Unaudited)

	Six Months ended Aug. 31, 2012	Six Months ended Aug. 31, 2011	Period from Inception (July 22, 2009) to Aug. 31, 2012
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	\$ (1,223,355)	\$ (537,200)	\$ (4,065,255)
Adjustments to reconcile net loss to net cash used in operating activities			
Shares issued for services	11,075	—	769,910
Depreciation	5,413	328	6,684
Warrant expense	—	—	149,999
Changes in assets and liabilities			
Accounts receivable	—	(1,579)	—
Accounts payable	(131,750)	3,741	160,109
NET CASH USED IN OPERATING ACTIVITIES	(1,338,617)	(534,710)	(2,978,553)
CASH FLOWS FROM INVESTING ACTIVITIES			
Certificate of deposit	(250,182)	—	(250,182)
Purchase of equipment	(38,812)	—	(59,291)
NET CASH USED IN INVESTING ACTIVITIES	(288,994)	—	(309,473)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from subscription receivable	865,000	—	865,000
Proceeds from sale of common stock	855,000	330,857	3,393,755
NET CASH PROVIDED BY FINANCING ACTIVITIES	1,720,000	330,857	4,258,755
NET INCREASE (DECREASE) IN CASH	92,389	(203,853)	970,729
Cash at the beginning of the year	878,340	242,256	—
Cash at the end of the year	\$ 970,729	\$ 38,403	\$ 970,729
SUPPLEMENTAL DISCLOSURES:			
Interest Paid	\$ —	\$ —	\$ —
Income taxes paid	\$ —	\$ —	\$ —
NON-CASH TRANSACTIONS:			
Subscriptions receivable	\$ 25,000	\$ —	\$ 890,000

Source: MetaStat, Inc.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by MetaStat, Inc. (“MetaStat” or “the Company”) with the assistance of Crystal Research Associates, LLC (“CRA”) based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in MetaStat’s statements on Forms 10-K, 10-Q, and 8-K, as well as other forms filed from time to time.

The content of this report with respect to MetaStat has been compiled primarily from information available to the public released by the Company through news releases, Annual Reports, and U.S. Securities and Exchange Commission (SEC) filings. MetaStat is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by MetaStat or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of forty thousand dollars and one hundred and fifty thousand warrants for its services in creating this report, for updates, and for printing costs. A selection of risk factors related to MetaStat’s business, intellectual property, and stock price is provided on the accompanying pages. For more complete information about the risks involved in an investment in the Company, please see MetaStat’s most recently filed Form 10-K for the fiscal year ended February 29, 2012: http://www.sec.gov/Archives/edgar/data/1404943/000141588912000892/mtst10k_feb292012.htm.

Investors should carefully consider the risks and information about MetaStat’s business, as described in the Company’s Form 10-K filed with the SEC on February 29, 2012, and overviewed below. Investors should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. The risks and uncertainties overviewed in MetaStat’s Form 10-K and below are not the only risks that the Company faces. Additional risks and uncertainties not presently known to MetaStat or that it currently believes to be immaterial may also adversely affect the Company’s business. If any of such risks and uncertainties develops into an actual event, MetaStat’s business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company’s shares could decline.

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A Selection of Risk Factors Related to MetaStat’s Business, Intellectual Property, and Stock Price

- MetaStat is at an early stage of development and does not have, and may never have, any products that generate revenues.
- MetaStat has a history of losses, and expects to incur net losses for the foreseeable future.
- MetaStat expects to continue to incur significant research and development expenses, which may make it difficult for the Company to achieve profitability.
- The Company does not have its own research facilities and will be dependent on third parties for product development.
- In addition to the funds raised in the Company’s recent private placements, MetaStat may be required to raise additional capital to complete the development and commercialization of its current and future product candidates. If MetaStat fails to obtain additional financing, it may be unable to complete the development and commercialization of product candidates or continue research and development programs.

- If third-party payors, including managed care organizations and Medicare, do not provide reimbursement or rescind their reimbursement policies for the Company's products, the products' commercial success could be compromised.
- MetaStat may experience delays in clinical trials that could adversely affect its financial position and commercial prospects.
- Adverse events in clinical trials may force the Company to stop development of its product candidates or prevent regulatory approval, if needed, of the product candidates.
- If the Company's product candidates do not meet safety or efficacy endpoints in clinical evaluations, they will not receive regulatory approval and MetaStat will be unable to market them.
- If the FDA were to begin regulating the Company's MetaSite *Breast* test, MetaStat could experience significant delays in commercializing the test, be forced to stop sales, experience significant delays in commercializing any future products, incur substantial costs and time delays associated with meeting requirements for pre-market clearance or approval, as well as experience decreased demand for its products and demand for reimbursement of its products.
 - Clinical laboratory tests, such as the MetaSite *Breast* test, are regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as administered through the CMS, as well as by applicable state laws. Diagnostic kits that are sold and distributed through interstate commerce are regulated as medical devices by the FDA. Clinical laboratory tests that are developed and validated by a laboratory for its own use are called laboratory development tests (LDTs). Most LDTs currently are not subject to FDA regulation, although reagents or software provided by third parties and used to perform LDTs may be subject to regulation. MetaStat believes that the MetaSite *Breast* test is not a diagnostic kit and also believes that it is an LDT. As a result, the Company believes the MetaSite *Breast* test should not be subject to regulation under established FDA policies. The FDA may decide at any time at its sole discretion to modify these rules, or the U.S. Congress may enact new legislation, resulting in the need for the Company to conduct further trials in order to qualify the MetaSite *Breast* test for marketing approval.
- If MetaStat was required to conduct additional clinical trials prior to marketing its diagnostic tests, those trials could lead to delays or failure to obtain necessary regulatory approvals and harm the Company's ability to become profitable.
- Complying with numerous regulations pertaining to the Company's business is a costly and time-consuming process, and any failure to comply could result in substantial penalties.
- Initially the Company's financial results will depend on sales of one test, the MetaSite *Breast* test, and MetaStat will need to generate sufficient revenues from this and other diagnostics or therapies to run its business.
- MetaStat may experience limits on revenues if physicians decide not to order the Company's tests.
- MetaStat may experience limits on revenues if patients decide not to use the Company's tests.
- If MetaStat is unable to develop products to keep pace with rapid technological, medical, and scientific change, the Company's operating results and competitive position would be harmed.
- If MetaStat becomes subject to product liability claims, the damages may exceed insurance coverage levels.
- If MetaStat is unable to develop adequate sales, marketing, or distribution capabilities or enter into agreements with third parties to perform some of these functions, it will not be able to commercialize its products effectively.
- In the future, MetaStat may rely on third-party manufacturers. The Company may be unable to control the availability or cost of producing its products.

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- MetaStat may enter into relationships with selected biotechnology companies to help develop and commercialize the Company's product candidates, especially in the field of therapeutics. If MetaStat does not find development and commercialization collaborators for its product candidates, it may have to reduce or delay the rate of product development and commercialization and increase expenditures.
 - Once MetaStat has a laboratory facility, it will be the Company's sole laboratory facility and should it become inoperable, the Company will be unable to perform its test and its business will be harmed.
 - Changes in healthcare policy could subject the Company to additional regulatory requirements that may interrupt commercialization of the MetaSite *Breast* test and increase the Company's costs.
 - MetaStat relies on a limited number of suppliers or, in some cases, a sole supplier, for some of its laboratory instruments and materials and may not be able to find replacements in the event the Company's supplier no longer supplies that equipment.
 - The Company's success depends on retention of its founder and other key personnel.
 - The Company's corporate compliance program cannot guarantee that MetaStat is in compliance with all potentially applicable regulations.
 - The Company's operations may involve hazardous materials, and compliance with environmental laws and regulations is costly.
 - If MetaStat uses biological and hazardous materials in a manner that causes injury, it could be liable for damages.
 - If MetaStat is unable to protect its intellectual property, it may not be able to compete effectively.
 - Litigation or third-party claims of intellectual property infringement could impair the Company's ability to develop and commercialize its products successfully.
 - The Company's rights to use technologies licensed from third parties are not within its control, and MetaStat may not be able to sell its products if it loses existing rights or cannot obtain new rights on reasonable terms.
 - Insiders have substantial control over the Company, and they could delay or prevent a change in corporate control even if other stockholders wanted it to occur.
 - MetaStat cannot offer assurances that its Common Stock will become liquid or that it will be listed on a securities exchange. In addition, there may not be sufficient liquidity in the market for the Company's securities in order for investors to sell their securities.
 - In order to raise sufficient funds to expand operations, MetaStat may have to issue additional securities at prices that may result in substantial dilution to the Company's shareholders.
 - The market price of the Company's Common Stock may be volatile.
 - Because MetaStat became a public company by means of a "reverse merger," it may not be able to attract the attention of major brokerage firms and will also be subject to a one-year "seasoning period" before it will be permitted to list securities on a securities exchange.
 - If MetaStat fails to maintain an effective system of internal control over financial reporting, it may not be able to accurately report financial results. As a result, current and potential investors could lose confidence in the Company's financial reporting, which could harm its business and have an adverse effect on stock price.
 - The Company's Common Stock is considered "penny stock." The market for penny stocks has experienced numerous frauds and abuses, which could adversely impact investors in the Company's stock.
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Glossary

Actin—An important structural molecule for the cytoskeletons of many eukaryotic cells.

Adenocarcinoma—A malignant tumor formed from glandular structures in epithelial tissue.

Assay (Technologies)—Used to make such isolated biomolecules, such as the DNA of a specific virus, visible for subsequent analysis.

Blank Check Company—A development-stage company that has no specific business plan or purpose or has indicated that its business plan is to engage in a merger or acquisition with an unidentified company or companies, other entity, or person. These very small companies typically involve speculative investments and often fall within the SEC's definition of penny stocks or are considered microcap stocks.

Chemotactic—Pertaining to a tendency of cells to migrate toward or away from certain chemical stimuli.

Chemotherapy—Medications given to kill or slow the growth of cancer cells. Chemotherapy is often used with surgery or radiation to treat cancer when the cancer has spread, when it has come back (recurred), or when there is a strong chance that it could recur.

Ductal Carcinoma—The most common type of breast cancer. It begins in the cells that line the milk ducts in the breast.

Epidermal Growth Factor (EGF)—A protein that stimulates normal cell growth, cancerous cell growth, and wound healing. Significant elevations of EGF have been implicated in the development and progression of solid tumors, including those of the lung, breast, prostate, colon, ovary, head, and neck.

Epithelial—Part of the epithelium, a thin layer of tissue that covers organs, glands, and other structures within the body.

Extracellular Matrix—A term used to describe the surrounding substance or environment of a cell.

Fine Needle Aspiration—The use of a thin needle to withdraw material from the body for analysis. The aspirated material is examined under the microscope by a pathologist.

Glycoproteins—Proteins that have an attached carbohydrate. Glycoproteins have appeared in most every biological process.

Hematogenous—Concerned with the production of blood or of one or more of its constituents, or taking place or spreading by way of the blood.

HER2/neu—A protein that indicates aggressive cancer, which is found in 30% of breast cancer patients.

Immunostaining—The staining of a specific substance by using an antibody against it that is complexed with a staining medium.

Invadopodia—Protrusions in the cell membrane of some cells that are rich in actin and extend into the extracellular matrix.

Invasion—The spread of malignant cells to new sites in the body.

Isoforms—A protein isoform is any of several different forms of the same protein.

Lymphatic System—A system of vessels and lymph nodes separate from the circulatory system that returns fluid and protein to the blood.

Lymphovascular Invasion—The invasion of cancer cells into blood vessels and/or the lymphatic system.

Macrophage—A white blood cell that helps the body defend itself against disease by surrounding and destroying foreign organisms.

Mechanisms—The natural or established processes by which cancer is brought about.

Mena—A protein that has a role in regulating cell movement, shape, and adhesion. The Mena protein is found in excessive amounts in tumors and is known to help cancer cells move away from a tumor and spread around the body to form secondary cancers—one of the main obstacles in treating cancer.

Metastasis—The spread of cancer to another part of the body, where it can form a secondary tumor.

Metastatic—Cancer that has spread to other parts of the body from the original tumor site.

Motility—The ability to move spontaneously and independently.

Perivascular—Situated or occurring around a blood vessel.

Personalized Cancer Therapies—Treatments tailored to a patient's specific needs based on genetic abnormalities found in the individual's tumor.

Polyoma Middle T Oncogene (PyMT)—A mouse line that has been engineered to be genetically predisposed to highly metastatic breast cancer.

Prognostic—Predicting the likely outcome of a disease; of or relating to a prognosis.

Protrusion—A bulge or projection from an object.

Radiation Therapy—A cancer treatment in which radiation energy is focused onto a specific area of the body to eradicate cancer cells and shrink tumors. Normal cells are less likely to be damaged by the radiation and are better able to repair themselves

Sample (Technologies)—Used to isolate and process DNA, RNA, and proteins from biological samples, such as blood or tissue.

Systemic—A disease or symptom that affects many different parts of the body.



CRYSTALRESEARCH
A S S O C I A T E S

EXECUTIVE INFORMATIONAL OVERVIEW®

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Crystal Research Associates is led by veteran Wall Street sell-side analyst Jeffrey Kraws, who is well known by the international financial media for his years of work on Wall Street and for providing consistent award-winning analyses and developing long-term relationships on both the buy-side and sell-side. He has been consistently ranked on Wall Street among the Top Ten Analysts for pharmaceutical stock performance in the world for almost two decades as well as ranked as the Number One Stock Picker in the world for pharmaceuticals by Starmine and for estimates from Zacks. Additionally, Mr. Kraws has been 5-Star ranked for top biotechnology stock performance by Starmine.

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