Zacks Small-Cap Research

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Brian Marckx, CFA
bmarckx@zacks.com
Ph (312) 265-9474

scr.zacks.com

10 S. Riverside Plaza, Chicago, IL 60606

Metastat Inc (MTST-OTC)

MTST: Q3 Results, Initial Test Launch Expected in 2016

Current Recommendation	**Buy**
Prior Recommendation	Hold
Date of Last Change	11/05/2015
Current Price (01/18/16)	$4.25
Target Price	**$11.00**

OUTLOOK

MTST, in collaboration with some of the leading cancer research institutions, discovered the critical roll that the Mena protein appears to play in cancer metastasis. MetaSite Breast and MenaCalc Breast, in late stage development, identify the presence of Mena and tumor microenvironments which have been shown in clinical studies to be associated with cancer metastasis. Performance looks to be superior to already commercialized metastatic-risk based diagnostics. MTST hopes to launch their breast cancer tests in 2016. MenaCalc is a platform technology which MTST hopes to exploit and launch follow-on tests for cancers of the lung (positive clinical data just reported), prostate and colon.

SUMMARY DATA

52-Week High	**$11.39**
52-Week Low	**$3.22**
One-Year Return (%)	**-44.42**
Beta	**0.71**
Average Daily Volume (sh)	**292**
Shares Outstanding (mil)	**2**
Market Capitalization ($mil)	**$8**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**9**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High,**
Type of Stock	**N/A**
Industry	**Med Products**

ZACKS ESTIMATES

Revenue
(in 000s of $)

	Q1 (May)	Q2 (Aug)	Q3 (Nov)	Q4 (Feb)	Year (Feb)
2015	0 A	0 A	0 A	0 A	0 A
2016	0 A	0 A	0 E	0 E	0 E
2017					1,467 E
2018					5,893 E

Earnings per Share

	Q1 (May)	Q2 (Aug)	Q3 (Nov)	Q4 (Feb)	Year (Feb)
2015	-$0.85 A	-$2.53 A	-$0.79 A	-$0.47 A	-$4.96 A
2016	-$1.21 A	-$0.73 A	-$1.03 E	-$1.07 E	-$4.12 E
2017					-$2.61 E
2018					-$1.92 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT's NEW…..

Q3 10-Q Filed:

MTST filed their 10-Q for the third quarter ending November 30, 2015. Operating expenses, of $1.1M, were well below our $1.8M estimate. The difference mostly attributable to lower than anticipated stock-based compensation and resulting in better than modeled operating loss ($1.2M A vs $1.8M E).

We have made only small changes to our model – mostly related to slight downward revisions to OpEx in Q4. We still expect to see a meaningful uptick in R&D expense as additional breast cancer trials get underway. MTST expects to have at least three additional breast cancer related clinical studies completed during 2016 to complement the already compelling data from recent studies. Launch of the initial test(s) are still expected to happen in 2016.

Q3 net loss and EPS were $1.3M and ($0.72), compared to our $1.9< and ($1.03) estimates. Cash balance stood at just $265k at Q3 quarter-end which the company expects to be sufficient to fund operations until the end of the current month (i.e. Jan 2016). We have previously and continue to incorporate the assumption that MTST raises additional capital via the sale of common equity and/or convertible debt.

Update: CLIA Certification, Presentation at AACR of Accuracy of MetaSite Breast

In late November, shortly following receipt of Massachusetts state licensure, MTST announced that they received CLIA certification from CMS for their Boston-based digital immunochemistry lab. The company now expects to launch their initial breast cancer assay(s) in the second half of this year.

The state licensure and CLIA certification follows on the heels of studies validating the performance and accuracy of MTST's fully automated MetaSite Breast assay. In late August MTST announced the automated (i.e. – to-be commercialized) MetaSite Breast assay showed greater than 97% analytical precision with a mean percent coefficient of variation of 6.6% (n=35) as compared to results of the Rohan et al study. This validation study was **presented at the American Association for Cancer** Research in Austin, Texas in early December.

As a reminder, the Rohan et al study, which included 481 patients with breast cancer, showed a highly statistically significant (95% C.I., p=0.004) association between risk of metastasis and MetaSite score in women with ER-positive/HER2-negative breast cancer. This represented a 2.7x increase in the odds of metastasis for women with a high risk score compared to those with a low risk score. In addition, for every increase of 10 MetaSites, there was a 1.16x increase in the risk of metastasis in this sub-population.

Additional confirmation of the accuracy and performance of the automated assay came in late September when MTST announced topline results from an independent study which also showed that MetaSite score was significantly associated with risk of distant metastasis in women with ER-positive/HER2-negative breast cancer. The data, which also confirmed results from Rohan et al, met its primary endpoint and not only showed MetaSite score was significantly and directly associated with increased risk of distant metastasis for both high versus low MetaSite scores (OR = 3.4; 95%CI = 2.8-4.1; P=0.0002), it also showed statistically significant association of risk of cancer metastasis between low and intermediate scores (OR=3.24; 95%CI = 2.6-3.9; P=0.0006).

Validation of the accuracy of the automated test is a major milestone as this is the test that is expected to be commercialized.

MTST continues to conduct additional validation studies (including to predict response to chemotherapy) with data from the following various studies expected;

- Kaiser cohort MetaSite/MenaCalc combined: topline data expected Q1 2016
    - Define product specs and risk cut-points for combined MetaSite/MenaCalc score as compared to MetaSite score and/or MenaCalc score
    - Define the assay or assays to be used in subsequent validation studies
    - Primary endpoint is direct assoc. between risk of distant metastasis and MetaSite/MenaCalc score in ER+/HER2-, triple negative and/or HER2+ invasive breast cancer patients

- ECOG 2197 cohort validation study: topline data expected Q1 2016. This is the pivotal clinical validation study for MetaStat in early stage breast cancer

    - Compare MetaSite/MenaCalc scores with Oncotype DX's "recurrence score"
    - Primary endpoint is direct assoc. between risk of distant metastasis and MetaSite/MenaCalc score in ER+/HER2-, triple negative and/or HER2+ invasive breast cancer patients

- Chemo-predictive study: topline data expected Q2 2016
    - Evaluate ability of MenaCal/MetaSite Breast to predict response of adding adjuvant chemotherapy to hormonal therapy in ER+ patients
    - Primary endpoint is direct association between risk classification and benefit from chemotherapy comparing Kaplan-Meier survival curves of treatment with tamoxifen alone versus treatment with combo of tamoxifen and adjuvant chemotherapy for all patients and high, medium and low risk cohorts

Noteworthy are results of Genomic Health's **T**rial **A**ssigning **I**ndividua**L**ized **O**ptions for treatment (**Rx**), or TAILORx, trial. The study, which includes over 10k patients with node-negative, ER+/HER2- breast cancer, is assessing whether GHDX's OncoType DX assay can effectively stratify which cases will and will not respond to chemotherapy. Of the 10k plus patients, 16% had a low OncotypeDX recurrence score and were treated with only hormone therapy, 67% had an intermediate score and were randomized to either chemo or hormone therapy and 17% had a high score and were treated with both chemo and hormone therapy. The findings, presented at the European Cancer Congress in late September, found that 99.3% of patients with a low OncotypeDX recurrence score (and therefore were not treated with chemo) were disease-free after five years.

Given the significant physical and emotional side effects (as well as cost) of chemotherapy, being able to effectively identify those patients which can skip chemo is of high value to both practitioners and patients. While OncotypeDX appears to be able to stratify at least a portion of the patients, it's important to note that 67% (or 2 of 3) patients had an intermediate score which provides no actionable information (i.e. "will or will they not respond to chemo?").

MTST's technology, in already completed clinical trials, has demonstrated an "intermediate risk" grouping of approximately 27% (i.e. – much better than OncotypeDX's). While these have not been chemo-predictive studies, these results may bode well for MetaSite/MenaCalc Breast providing a tighter range of intermediate risk patients, therefore offering a diagnostic that would have utility for a greater portion of the ER+/HER2- breast cancer population and clinicians more actionable information. MTST's chemo-predictive study (summarized above) should provide much greater insight into how MetaSite/MenaCalc breast stacks up against OncotypeDX in this indication.

We are reiterating our Buy recommendation and $11/share price target.

BACKGROUND

Breast Cancer
Breast cancer is one of the most prevalent malignant disease in the U.S. and is the second most common cause of death of women. According to the American Cancer Society there were approximately 300k incidences of breast cancer in 2013 and ~40k related deaths.

Breast cancer comes in many forms and is diagnosed using a several characteristics to define (i.e. "stage") the tumor and the risk of metastasis, which in turn is used to help guide treatment decisions. These characteristics include tumor size, tumor grade, receptor status and angiolymphatic invasion, among others.

- Tumor grade: refers to the similarity of the cancer cells to normal tissue. The less similar, the higher the grade and, generally the worse the prognosis
- Angiolymphatic invasion: refers to cancer which has spread to the lymph nodes
- Receptor status (or molecular subtype): identifies the tumor by which hormone receptors are involved in the cancer growth. This includes estrogen receptors (ER), progesterone receptors (PR) and HER2 (human epidermal growth factor receptor 2). Receptor status is used to determine if certain targeted hormone therapies are appropriate, such as tamoxifen,and trastuzumab, which target specific receptors. Molecular subtypes are further characterized as Luminal A, Lumina B or HER2 enriched
    - Luminal A: accounts for 40% - 60% and is the most common form of breast cancer. Tends to be ER-positive and/or PR-positive and HER2-negative
    - Luminal B: accounts for 5% - 20%. Also typically ER-positive and/or PR-positive but HER2-positive. Luminal A and B, expressing ER+ and PR+ can typically be treated with targeted hormone therapies which, while shown to improve the short term prognosis, has not demonstrated better long-term survival than other subtypes
    - Triple-Negative (or basal): accounts for 5% - 20%. ER-negative, PR-negative and HER2-negative which means there are no targeted hormone therapies to treat these tumors and, generally, prognosis is poorer
    - HER2 Enriched: accounts for ~10%. Produces excess HER2 but are ER and PR negative. Typically have poorer short-term prognosis than ER and PR positive due to lack of hormone therapy options

Cancer Metastasis
Cancer-related death is overwhelmingly the result of distant metastasis and this is particularly true for breast cancer. But while strong theories exist for the reasons and causes of metastasis (Greek for "displacement"), consensus remains fleeting. What is known is that the metastatic process involves the primary tumor shedding cancer cells either into the lymphatic system or blood vessels where they are then able to circulate to other parts of the body.

However, how, why and where in the body these cancer cells will grow into a secondary tumor is still not fully understood. One widely held theory, proposed by an English Surgeon, Stephen Paget, in the late 1800's, suggests that cancer cells will only grow in areas that are predisposed to tumor growth. This is known as the "seeds and soil" hypothesis with tumor cells representing the seeds and the predisposed metastatic site representing the "congenial soil." This hypothesizes that migration takes place by single cancer cells individually penetrating blood vessels, traveling through the body and then adhering to "congenial soil". Additional research has suggested that cancer cells that break away from the primary tumor may bring along with them "soil" which can then act as the initial fertilizer for a secondary tumor to grow.

As MTST believes (based on supporting preclinical and clinical data), and as we discuss below, a tumor microenvironment consisting of three specific types of cells, is responsible for one of the most important initial metastatic processes and explains how, why and where the primary tumor cells enter the bloodstream. This tumor microenvironment of metastasis (TMEM) theory has garnered significant attention (in mainstream and healthcare media and by leading cancer researchers), particularly following the recent publication of clinical trial data that demonstrated TMEM may be a reliable predictor of cancer metastasis.

Cancer Is Often Over-treated, Resulting in Adverse Physical, Emotional and Financial Consequences
Today, many cancer diagnoses result in inappropriately-aggressive treatment. This is because most tumors are not capable of metastasis yet there is not a reliable diagnostic to differentiate between invasive and indolent forms of

the disease. So, by default, most cancer patients will receive chemotherapy (in a "better to be safe than sorry" approach) when less aggressive local treatment such as surgery, targeted hormone therapy and radiation may have been sufficient in the majority of cases. MetaStat's diagnostic products address this problem of overtreatment – which can add significant expense and is associated with severe toxic side effects.

In cases where the cancer has spread to distant sites (such as the liver, lungs and other organs) the malignancy almost always (~90% of the time) results in death. Chemotherapy can increase survival of breast cancer which has already spread with statistics indicating chemotherapy increases the 15-year survival rate by 10% in women younger than 50 and by about 3% in those aged 50 and older.[1] But while chemotherapy can be beneficial for systemic disease, only ~30% - 35% of breast cancers will metastasize and in the majority of cases, localized treatment without exposure to prophylactic chemotherapy may be most appropriate. Despite this, approximately 80% of all patients in the U.S. receive chemotherapy.

Chemotherapy targets growing cells, which includes cancer but also includes some normal healthy cells in the blood, intestines, mouth, hair and other areas of the body. This can cause serious and sometimes severe and highly debilitating side effects such as fatigue, pain, mouth sores, vomiting, certain blood disorders and damage to muscles and nerves. And while most side effects abate with discontinuance of chemotherapy, long-term and permanent damage to the organs (including heart, lungs and kidneys) and nervous system are also possible. And in addition to the harmful side effects of chemotherapy it is also expensive, costing an average of approximately $75k per patient. As such, there should be an inherent interest to incorporate chemotherapy into a treatment regimen only when the risk to the patient is outweighed by the benefit.

But, unless a reliable test becomes available to differentiate between invasive and indolent tumors, the majority of patients will continue to receive overly aggressive therapy, most of which may experience no benefit. And a reliable metastatic-risk based cancer diagnostic not only has utility in saving the majority of breast cancer patients the morbidity and mortality associated with chemotherapy and the health care system the cost, it also has the potential to alleviate otherwise significant psychological stress of patients if the tests determine a low risk of metastasis.

Mena Protein and Its Roll In Metastasis

The Mena (mammalian Ena homolog) protein is a type of enabled/vasodilator-stimulated phosphoprotein. Ena/VAS proteins are responsible for regulating cell motility (i.e. – movement of cells in specific directions to particular locations). Mena, in healthy individuals, is expressed during early embryogenesis and is a key participant in initial growth and development of the nervous system. Following birth, expression of Mena subsides. However, in all epithelial-based tumors the Mena-related gene is turned back on which can result in the accumulation of high concentrations of Mena protein and certain of its isoforms.

Discovery of the Mena protein's roll in enabling cancer metastasis and how this could be applied to clinical diagnostics has been developed through an almost two-decade relationship between some of the top global cancer-related research institutions including M.I.T., Albert Einstein College of Medicine, Cornell and IFO-Regina Elena Cancer Institute (Rome, Italy). The pivotal findings, which are incorporated into MTST's diagnostics technology, were a.) how the Mena protein enhances cell motility and invasiveness and b.) discovery of what the company calls the "MetaSite" – or the portal entry where the metastatic process is believed to take place.

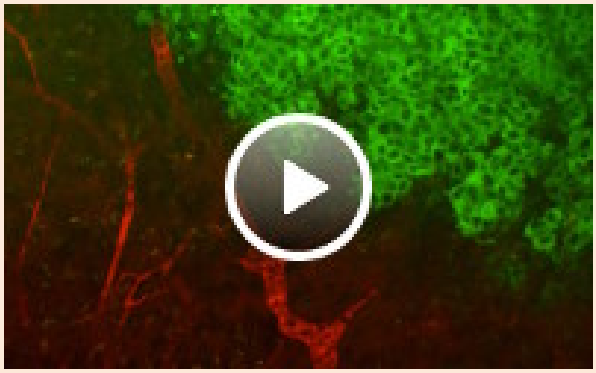
Key to these findings were that the Mena protein and its isoforms are highly influential in the strength and direction of tumor cell movement and that, most significantly, certain isoforms steer the cancer cells towards blood vessels where the cancer can then spread through the body.

There are several Mena protein isoforms. MTST has identified those which have most influence on the metastatic process; $Mena^{INV}$ (i.e. – invasive) and $Mena^{11A}$. $Mena^{INV}$ is the "bad" isoform and promotes cancer cell migration towards blood vessels and reduces adhesiveness to other cells. $Mena^{11A}$, by contrast, is the "good" isoform and has the effect of hindering the ability of cancer cells to separate from the tumor. MTST's MenaCalc assay measures the relative levels of these two Mena isoforms - relatively higher and lower levels of $Mena^{INV}$ and $Mena^{11A}$ indicate increased risk of metastasis.

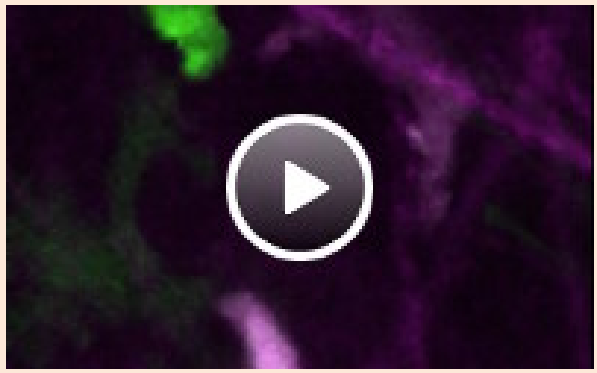
[1] Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* **365**, 1687–1717 (2005)

Video Imaging of the metastatic process (Ctrl+click to play video. Video addresses in footnotes)

Metastatic Cancer Cells Move Towards Blood Vessel[2]



Metastatic Cancer Cell Meets Macrophage[3]



Metastatic Cancer Cell Opening Blood Vessel Wall[4]



MetaSite: The moment of metastasis[5]



Breast Cancer Assays: *MetaSite Breast* and *MenaCalc Breast*

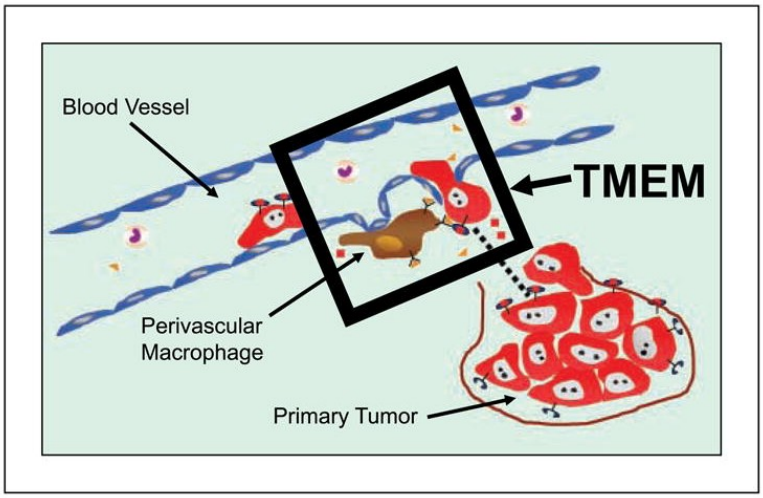
The company's initial diagnostic tests, MetaSite Breast and MenaCalc Breast, focus on metastatic risk of breast cancer. It is expected that this information will be used by oncologists to make more informed treatment decisions, including whether the use of aggressive therapy such as prophylactic chemotherapy is appropriate. Both tests utilize common and widely used antibody-antigen detection methods which is expected will help keep manufacturing and production costs to a minimum (and help maximize margins).

MetaSite Breast identifies and quantifies Tumor Microenvironment of Metastasis (TMEM) sites, or what the company calls "MetaSites". These MetaSites are where the metastatic process is believed to take place (i.e. – where the tumor cells enter a blood vessel) and which are characterized by the assemblage and direct contact of three specific types of cells; an endothelial cell (which line blood vessels), a perivascular macrophage (type of

[2] MetaStat.com. http://content.stockpr.com/metastat/db/Videos/984503/video_file/video2.mp4
[3] MetaStat.com. http://content.stockpr.com/metastat/db/Videos/984523/video_file/video4.mp4
[4] MetaStat.com. http://content.stockpr.com/metastat/db/Videos/984543/video_file/video6.mp4
[5] MetaStat.com. http://content.stockpr.com/metastat/db/Videos/984553/video_file/video7.mp4

immune cell around blood vessels) and a tumor cell that expresses the Mena protein. MTST has shown in clinical studies that the density of these MetaSites is positively correlated to metastatic risk.

MetaSite Illustration



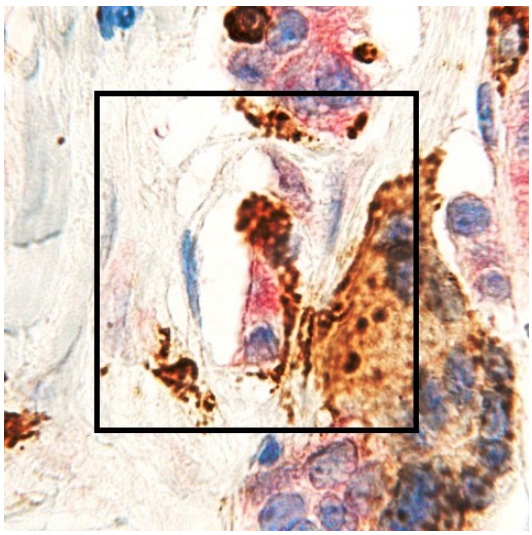
SOURCE: Footnote[6]

MetaSite Breast utilizes immunohistochemistry, a digital antigen detection technique whereby specific antibody-based stains are introduced to the sample and cells of interest are visible as the stained antibodies bind to a corresponding antigen. MetaSite Breast is performed on formalin fixed paraffin embedded (FFPE) biopsy tissue which is treated with a triple stain – a blue stain to label the endothelial cell, a brown stain to label the perivascular macrophage and a red stain to label the Mena protein-expressing tumor cell. The sample is viewed with a high powered microscope and the number of MetaSites are counted. The result is a MetaSite score which correlates to risk of metastasis.

The test can be performed relatively rapidly, with expected typical turnaround time of about 3 – 5 days. MetaSite Breast will stratify patients to low, moderate or high risk of developing metastatic breast cancer within ten years of diagnosis. These results are then expected to be used by physicians and patients in determining the most appropriate course of treatment.

MetaSite

Endothelial cell (blue), Perivascular macrophage (brown) and Mena tumor cell (red) in direct contact



SOURCE: MetaStat Inc.

[6] Robinson B, et al. *Tumor Microenvironment of Metastasis in Human Breast Carcinoma: A Potential Prognostic Marker Linked to Hematogenous Dissemination.* Clin Cancer Res. 2009 Apr 1; 15(7): 2433–2441.

MetaSite Breast is expected to be applicable to ER-positive/HER2-negative early stage breast cancer patients. The ER-positive/HER2-negative cohort accounts for approximately 60% of all breast cancer patients, or approximately 140k in the U.S.

MenaCalc uses immunofluorescence (similar to immunohistochemistry but uses a fluorescent dyes to tag the antibody) to quantify the relative expression of the Mena protein and its isoforms. Clinical trials have demonstrated a positive association between expression of the non-invasive Mena isoform Mena^{11a} subtracted from the total Mena protein expression and risk of death from metastatic cancer.

MenaCalc can be used with both FFPE tissue or, more conveniently, with cells taken directly from the tumor with a fine needle. This allows the sample to be taken without requiring surgery. It is a platform technology which is applicable to several epithelial-based tumors including breast, lung, prostate and colorectal.

MenaCalc Breast is the first assay being developed on the MenaCalc platform, which is expected to be expanded to include assays for lung, prostate and colorectal cancers. MenaCalc Breast and MetaSite Breast can be used individually with each producing its own Metastasis Score or together, which will provide an integrated Metastasis Score – this combined score is expected to provide the most substantive information. While MetaSite Breast is applicable to the breast cancer subgroup which is ER-positive/HER-negative, MenaCalc Breast may be applicable to all breast cancer subtypes.

Patent Portfolio

The patent portfolio protecting the technology includes 13 filed and three issued U.S. patents, which were issued from late 2012 to early 2014. Estimated life of entity of the filed and issued patents extends to 2030.

Jurisdiction	Title	Type and Number	Filing Date
U.S.	**Tumor microenvironment of metastasis (TMEM) and uses thereof in diagnosis, prognosis, and treatment of tumors**	**U.S. Patent No. 8,642,277**	**Issued: 2/4/2014**
U.S.	**Metastasis specific splice variants of Mena and uses thereof in diagnosis and prognosis and treatment of tumors**	**U.S. Patent No. 8,603,738**	**Issued: 12/10/2013**
U.S.	**Isolation, gene expression, and chemotherapeutic resistance of motile cancer cells**	**U.S. Patent No. 8,298,756**	**Issued: 10/30/2012**
U.S.	Metastasis specific splice variants of Mena and uses thereof in the treatment of tumors	U.S. Patent Application No. 14/074,089 Divisional of U.S. Pat. Appl. No. 12/462,324	Filed: 11/7/2013 Priority Date: 2/2/2007
Europe	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	Patent Application No. 08713370.8	Filed: 1/31/2008
Canada	Metastasis specific splice variants of Mena and uses thereof in diagnosis, prognosis and treatment of tumors	Patent Application No. 2,676,179	Filed: 1/31/2008
Canada	Isolation, gene expression, and chemotherapeutic resistance of motile cancer cells	Patent Application No. 2,576,702	Filed: 8/4/2005
Europe	Method for identifying metastasis in motile cells	European Patent No. 1784646 Application No. 05807467.5	Filed: 8/4/2005 Publication: 6/13/2012
U.S.	Human invasion signature for prognosis of metastatic risk	U.S. Patent Application No. 14/115,928	PCT Filed: 11/15/2012
U.S.	Alternatively spliced mRNA Isoforms as prognostic indicators for metastatic cancer	U.S. Patent Application No. 14/000,995	Filed: 2/24/2012
Europe	Alternatively spliced mRNA Isoforms as prognostic indicators for metastatic cancer	Patent Application No. 12749944.0	Filed: 2/24/2012
Singapore	Alternatively spliced mRNA Isoforms as prognostic indicators for metastatic cancer	Patent Application No. 201306378-9	Filed: 2/24/2012

SOURCE: MetaStat Inc.

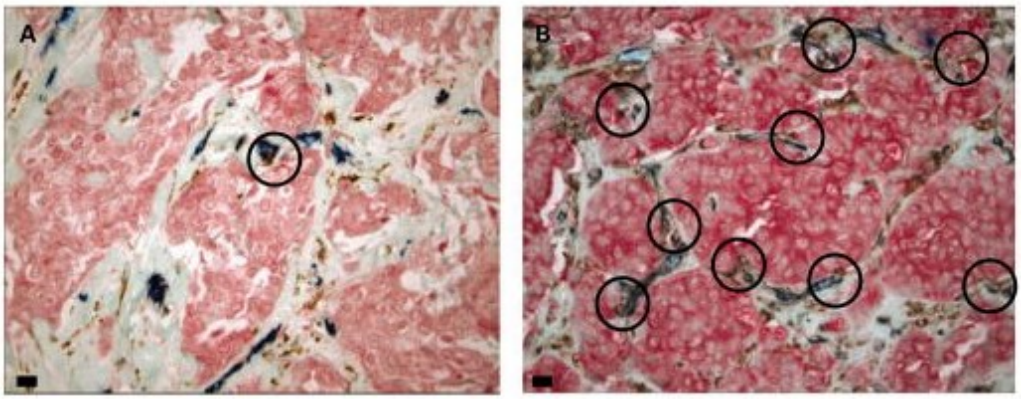
CLINICAL DATA

Clinical Data: ***Published in peer-reviewed journals. Evidence supports utility in breast and lung cancers…*** MetaSite Breast and MenaCalc Breast have been validated in three and two human studies, respectively which, in aggregate include approximately 1,800 patients. And, most recently MenaCalc Lung was used in a clinical study (n=201), results of which showed that high MenaCalc scores were predictive of overall survival in non-small cell lung cancer patients. MTST expects to conduct additional prognostic and chemo-predictive clinical trials during 2015, including at least three more in breast cancer in order to provide further support of the technology in what the company expects will be their initial commercial indication.

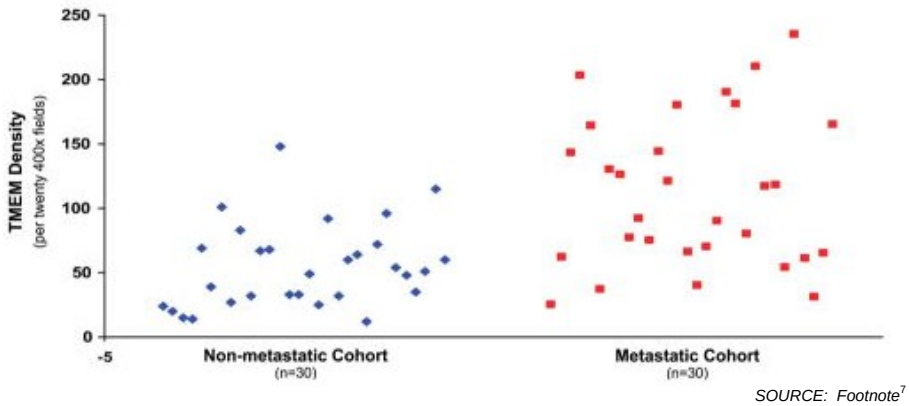
MetaSite Breast: Predictive of metastasis in ER-positive/HER2-negative breast cancer

- **60-Patient, Retrospective Study:** the first human study with MetaSite Breast was a 5-year retrospective study which included 60 women; 30 pairs of women were matched for age, tumor size and grade, lymphovascular involvement and hormone status (ER, PR, Her2/Neu status). Results, which were published in 2009 in the peer-reviewed journal Clinical Cancer Research, showed MetaSite density (i.e. – number of MetaSites in a given area) was greater in women that developed metastatic disease. The difference, as compared to those women where the cancer remained localized, was highly statistically significant (median density of 150 versus 50, p = 0.00006). The number of MetaSites ranged from a low of 12 to a high of 240. Results further showed that for every increase of 10 MetaSites, the odds of metastasis increased by 1.9x (i.e. – almost doubled). In addition, it was found that there was no correlation between MetaSite density and patient clinical make-up.

MetaSites are circled: Image "A" (left) from non-metastatic patient, image "B" (right) from metastatic patient



Individual MetaSite densities of each patient (n=60). Median density of non-metastatic and metastatic were 150 and 50, respectively



SOURCE: Footnote[7]

[7] Robinson B, et al. *Tumor Microenvironment of Metastasis in Human Breast Carcinoma: A Potential Prognostic Marker Linked to Hematogenous Dissemination.* Clin Cancer Res. 2009 Apr 1; 15(7): 2433–2441.

- **481-Patient, Retrospective-Prospective Study (aka Rohan *et al* study):** the second and most recent study using MetaSite Breast was a prospective study which included tumor samples from 481 patients who were diagnosed with breast cancer between 1980 and 2000 and developed a distant metastasis. Patients were followed through 2010. Results were published in August 2014 in the Journal of the National Cancer Institute. 259-patient pairs were matched (control included 222 patients: 189 which were used once, 29 used twice and 4 used three times) for age at and calendar year of diagnosis. There was no association between TMEM score (i.e. – MetaSite score/density) and tumor size or number of positive lymph nodes.

  MetaSite cutpoints were predefined as high-risk, medium-risk and low-risk based on the number of MetaSites present. For the entire patient population, risk of metastasis increased with higher MetaSite scores, although this was not statistically significant. Also, in the triple-negative and HER2-positive subgroup MetaSite score was not associated with metastatic risk. However, in the subgroup of women with ER-positive/HER2-negative breast cancer (n = 295: 147 case patients, 148 control) there was a highly statistically significant (95% C.I., p=0.004) association between risk of metastasis and MetaSite score. This subgroup represents approximately 60% of all breast cancers. This represented a 2.7x increase in the odds of metastasis for women with a high risk score compared to those with a low risk score. In addition, for every increase of 10 MetaSites, there was a 1.16x increase in the risk of metastasis in this sub-population.

Statistically Significant Association Between MetaSite Density and Metastatic Risk in ER-Positive/HER2-Negative Subgroup

Table 2. Association between tumor microenvironment of metastasis (TMEM) score and risk of distant metastasis, overall and by tumor subtype

				Odds ratio (95% confidence interval)†	
Tumor type	**TMEM category**	**Case subjects, No.***	**Control subjects, No.**	**Univariate**	**Multivariable**
All subjects	≤6	66	89	1.00 (referent)	1.00 (referent)
	7–22	71	85	1.14 (0.74 to 1.76)	1.13 (0.67 to 1.90)
	≥23	122	85	1.93 (1.26 to 2.97)	1.49 (0.86 to 2.56)
	P_{trend}			.002	.14
	Continuous, per 10 units			1.07 (1.01 to 1.13)	1.02 (0.95 to 1.10)
Triple-negative‡	≤6	20	16	1.00 (referent)	1.00 (referent)
	7–22	14	8	1.40 (0.46 to 4.25)	1.61 (0.46 to 5.59)
	≥23	22	18	0.98 (0.38 to 2.51)	0.73 (0.24 to 2.22)
	P_{trend}			.95	.58
	Continuous, per 10 units			0.93 (0.80 to 1.07)	0.88 (0.75 to 1.03)
ER+/HER2−	≤6	30	55	1.00 (referent)	1.00 (referent)
	7–22	41	53	1.42 (0.78 to 2.59)	1.32 (0.70 to 2.52)
	≥23	76	40	3.48 (1.95 to 6.22)	2.70 (1.39 to 5.26)
	P_{trend}			<.001	.004
	Continuous, per 10 units			1.19 (1.07 to 1.32)	1.16 (1.03 to 1.30)
HER2+	≤6	14	5	1.00 (referent)	1.00 (referent)
	7–22	13	10	0.46 (0.13 to 1.69)	0.68 (0.16 to 2.99)
	≥23	20	13	0.55 (0.16 to 1.94)	0.76 (0.17 to 3.34)
	P_{trend}			.41	.75
	Continuous, per 10 units			0.90 (0.76 to 1.05)	0.88 (0.73 to 1.06)

SOURCE: Footnote[8]

IHC4 (which was used as a surrogate for Oncotype DX) was also used with the study subjects. IHC4 is an already commercialized test for metastatic breast cancer risk which provides a score based on four markers; HER2 receptors, estrogen receptor, progesterone receptor and Ki-67 protein. IHC4 score was not estimable in the triple-negative and HER2 subgroups. In the ER-positive/HER2-negative subgroup the top two risk quartiles showed an association for increase in metastatic risk (60%) but this was not statistically significant. And while it did meet statistical significance on a continuous basis (i.e. - all quartlies included), it was just barely statistically significant and demonstrated a 6% increase in risk per 10-unit increase in the score.

[8] Rohan T., et al. *Tumor Microenvironment of Metastasis and Risk of Distant Metastasis of Breast Cancer*. J Natl Cancer Inst. 2014 June 3:106(8)

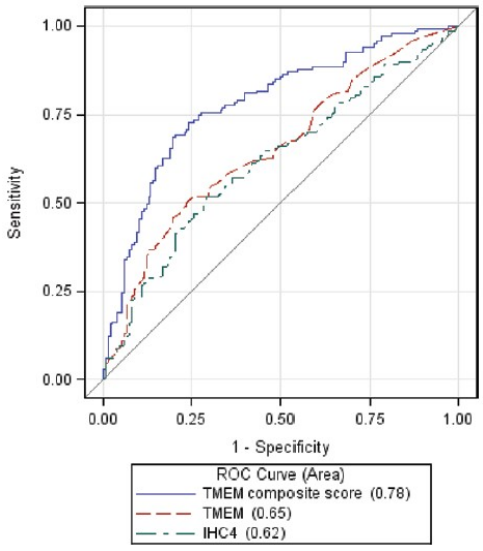
Table 3. Association between IHC4 score and risk of distant metastasis, overall, and by tumor subtype

Tumor type	IHC4 category	Case subjects, No.*	Control subjects, No.	Odds ratio (95% confidence interval)†	
				Univariate	Multivariable
All subjects	≤−7.81	49	86	1.00 (referent)	1.00 (referent)
	>−7.81 to 88.32	96	87	2.05 (1.27 to 3.32)	1.50 (0.84 to 2.67)
	>88.32	113	85	2.53 (1.55 to 4.11)	1.05 (0.55 to 2.01)
	P_{trend}			<.001	.93
	Continuous, per 10 units			1.06 (1.03 to 1.09)	1.01 (0.97 to 1.05)
Triple-negative‡	Continuous, per 10 units			0.91 (0.74 to 1.12)	0.90 (0.66 to 1.22)
ER+/HER2−	≤−7.81	49	71	1.00 (referent)	1.00 (referent)
	>−7.81 to 88.32	84	69	1.76 (1.10 to 2.84)	1.62 (0.94 to 2.81)
	>88.32	14	8	2.54 (0.97 to 6.62)	1.61 (0.48 to 5.47)
	P_{trend}			.01	.12
	Continuous, per 10 units			1.09 (1.03 to 1.15)	1.06 (1.00 to 1.13)
HER2+	Continuous, per 10 units			1.06 (0.94 to 1.20)	1.07 (0.92 to 1.24)

SOURCE: Footnote[9]

MetaSite and IHC4 were also modeled together (and adjusted for clinical variables; lymph node status, tumor size and grade, hormone therapy, age) which provided additional insight into the comparability, as well as potential difference in utility of the two tests. For one, it showed that MetaSite score was only weakly correlated with IHC4 (i.e. - indicates MetaSite score provides additional actionable information). But even more important was that there remained little difference to the results when the two tests were modeled individually with results again showing; a) a strong and statistically significant association between MetaSite score and metastasis and b) a non-statistically significant association between IHC4 score and metastatic risk but a barely statistically significant association between IHC4 score and metastatic risk when IHC4 was modeled as a continuous variable.

In this same subgroup a receiver operating characteristic (ROC) analysis was also done comparing MetaSite score, composite score and IHC4 score. The composite score combined the MetaSite score with clinical characteristics (tumor size, number of positive lymph nodes, tumor grade and hormone therapy) included as variables in the regression model. While comparison of MetaSite Score with IHC4 showed neither test to be statistically superior to the other, MetaSite composite score, as illustrated in the chart below, did have a higher specificity than IHC4. Neither MetaSite Breast or IHC4 was predictive of metastatic risk in triple negative or HER2-positive subgroups.



SOURCE: Footnote[10]

[9] Rohan T., et al. *Tumor Microenvironment of Metastasis and Risk of Distant Metastasis of Breast Cancer.* J Natl Cancer Inst. 2014 June 3:106(8)

[10] Rohan T., et al. *Tumor Microenvironment of Metastasis and Risk of Distant Metastasis of Breast Cancer.* J Natl Cancer Inst. 2014 June 3:106(8)

Results Confirmed with Automated Version of MetaSite Breast

In August 2015 MTSTS announced that th positive results from this Rohan et al. study were replicated with 97% analytical precision with their automated version of MetaSite Breast. Additional confirmation of the accuracy and performance of the automated assay came in late September when MTST announced topline results from an independent study which again showed that MetaSite score was significantly associated with risk of distant metastasis in women with ER-positive/HER2-negative breast cancer. The data, which also confirmed results from Rohan et al, met its primary endpoint and not only showed MetaSite score was significantly and directly associated with increased risk of distant metastasis for both high versus low MetaSite scores (OR = 3.4; 95%CI = 2.8-4.1; P=0.0002), it also showed statistically significant association of risk of cancer metastasis between low and intermediate scores (OR=3.24; 95%CI = 2.6-3.9; P=0.0006).

Validation of the accuracy of the automated test is a major milestone as this is the test that is expected to be commercialized. This should also bode well for eventual CLIA certification (Kaiser validation study will be used to support CLIA certification) – which the company anticipates could happen in Q1 2016.

JNCI Editorial Supports Further Investigation of MetaSites' Roll in "Poorly Understood" Metastatic Process

Publication of this 481-patient study data in JNCI was accompanied by an editorial supporting further investigation of MetaSite's roll in the metastatic process. The editorial, written by a group of PhD's/MD's from leading cancer hospitals and teaching institutions including Dana-Farber/Harvard/Mass General, is titled, *Seeds and Soil: Unraveling the Role of Local Tumor Stroma in Distant Metastasis*. Seeds and soil, as we discussed earlier, was a theory of cancer metastasis developed in the late 19th century that proposes single cancer cells from a primary tumor individually penetrate blood vessels and will grow into a secondary tumor only in areas of the body that are predisposed to tumor growth (i.e. – where there is congenial soil). The basis (which has been further built upon) of seeds and soil is still widely supported today.

The authors of this editorial note that, "metastatic progression remains a poorly understood process" and certain observations of cancer metastasis such as evidence of primary tumor stromal cells found in secondary tumors and incidences of initial lung metastases in the vasculature conflict with the basis of the seeds and soil theory. The authors note that, "the role of the TMEM [i.e. – MetaSite] in these contexts is unknown, but it is conceivable that it could play a role in the shedding of tumor fragments in circulation and growth and invasion at the secondary site."

The authors conclude by encouraging further study of MetaSite's roll in the metastatic process writing, "This overwhelming complexity of the metastatic process highlights the importance of mechanism-based, tumor-type specific studies in clinically relevant murine models. As done by Rohan *et al*. in the accompanying study, the findings should be validated in correlative clinical studies. This approach may greatly facilitate the development of efficacious anti-metastatic strategies." [11]

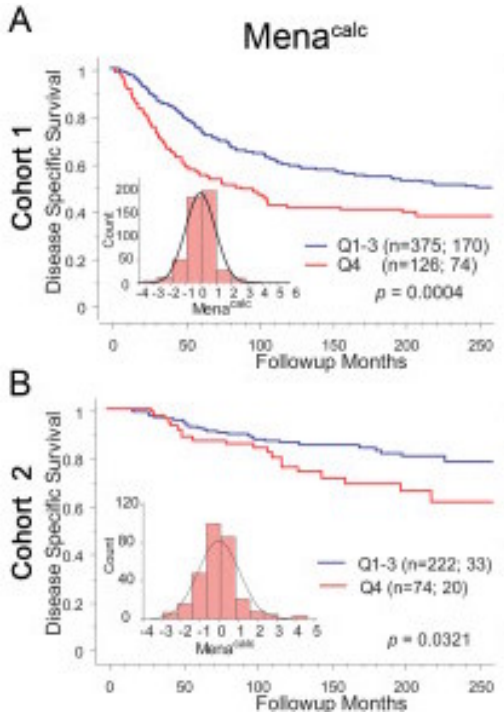
[11] Duda D. et al. *Seeds and Soil: Unraveling the Role of Local Tumor Stroma in Distant Metastasis*. JNCI J Natl Cancer Inst (2014) 106(8): dju187doi: 10.1093/jnci/dju187

MenaCalc Breast: Prognostic for disease-survival/metastasis in node positive/ER-negative breast cancer patients

- **797-Patient Study:** MenaCalc Breast was used in a 797-patient study to determine its ability to predict risk of disease-specific death. Two independent cohorts were analyzed; 501-patients and 296-patients, differing based on the range of years when they underwent surgery. A manuscript of the study, titled *Quantitative Assessment of Invasive Mena Isoforms (Mena^{calc}) as an Independent Prognostic Marker in Breast Cancer*, was published in 2012 in the journal Breast Cancer Research.

  Mena^{calc} is a measurement of all Mena isoforms excluding Mena^{11A} (i.e. – "good", or the anti-invasive Mena isoform). Mena^{calc} was used as a metric in this study to determine its association with metastasis in breast cancer. Antibodies for all isoforms of Mena and Mena^{11A} were used to determine their individual expression, the combination of which equates to a Mena^{calc} score.

  While results of the study showed expression of total Mena or Mena^{11A} were not associated with statistically significant risk of cancer death (which was used as a proxy for metastasis) in either cohort, when the study population was further segmented by Mena^{calc} scores, a strong association was found between the highest quartile of Mena^{calc} and poor outcomes (i.e. earlier death) – this was true for both cohorts individually as well as on a combined basis. When quartiled, Mena^{11A} and pan-Mena were not associated by themselves with disease-specific survival.



SOURCE: Footnote[12]

Mena^{calc} was also assessed in subgroups. In node-positive and ER-negative patients it demonstrated statistical significance in disease-specific survival, although not with node-negative and ER-positive patients.

Authors of the study (which includes stockholders of and consultants to MTST) concluded that, "Our results indicate that Mena^{calc} can be used successfully to stratify patients into high and low risk for developing metastasis. This test may have value in node positive, ER-negative patients which are not addressed by current, commonly used prognostic assays. Once validated in larger multi-institutional cohorts, this assay may

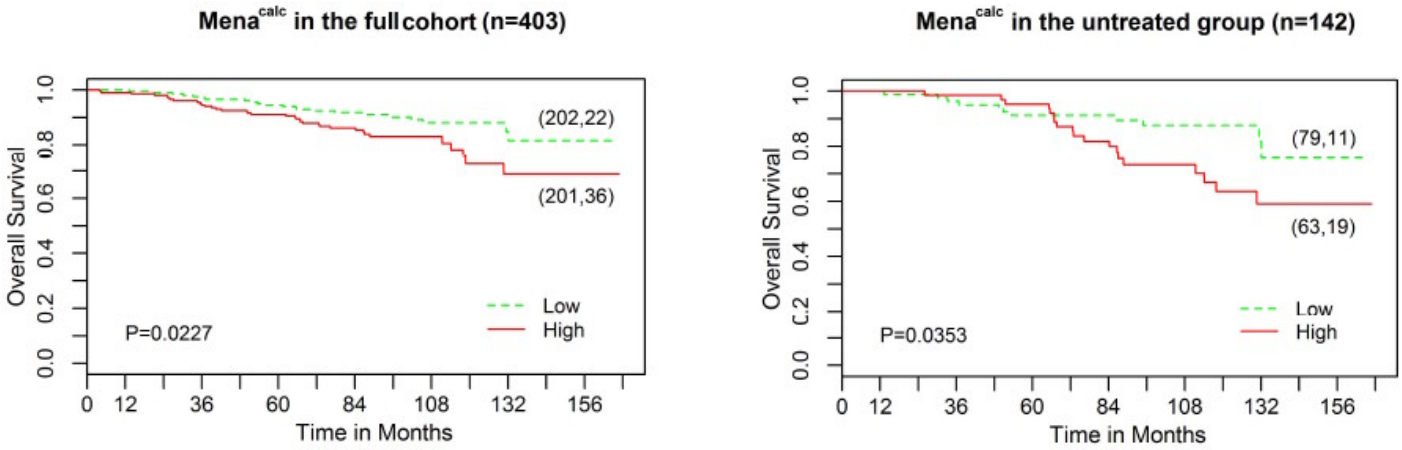
[12] Agarwal, S. et al. *Quantitative Assessment of Invasive Mena Isoforms (Mena^{calc}) as an Independent Prognostic Marker in Breast Cancer*. Breast Cancer Res. 2012; 14(5): R124

provide additional information to assist breast cancer oncologists in selecting appropriate therapy for their patients."

- **403-Patient Axillary Node-Negative Study:** MenaCalc was assessed in a 403-patient study to determine its utility as a prognostic for axillary node-negative (ANN) breast cancer. A manuscript of the study was published in the July 2015 issue of BioMed Central Cancer. Axillary lymph nodes are located in the armpit which is typically the first place where breast cancer will spread. ANN means that the cancer has not spread to the lymph nodes which generally relates to a more favorable prognosis. Tumor samples were obtained from eight Toronto hospitals where patients were treated from 1987 to 1993. Of the 403 patients, 332 had no lymphatic invasion while 70 did (data was missing on 1). Subgroups including treatment (chemo and/or hormone therapy, n=261)) versus non-treatment (n=142) and molecular subtype; luminal, basal and HER2, were also included in the analysis.

  Mena^{calc} scores were characterized as "high" if above the median and "low" if below the median and used to assess Mena^{calc} as a predictor of overall survival. The data showed that there was a significant association between high Mena^{calc} scores and increased risk of any-cause death (95% C.I., p=0.0199) in the full data set as well as in the non-treatment subgroup (95% C.I., p=0.0052). In addition, there was a trend towards (although not statistically significant) increased risk of all-cause death with high Mena^{calc} scores in all the three molecular subtype subgroups.

Statistically Significant Association With High Mena^{calc} Scores and Overall Survival in Full Cohort (L) and Untreated Subgroup (R)



SOURCE: Footnote[13]

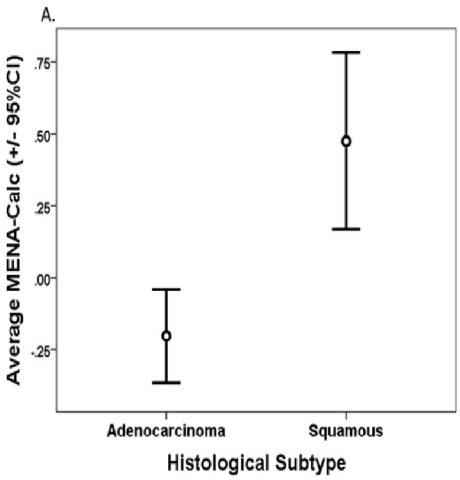
MenaCalc Lung: Significant association of MenaCalc Lung scores and metastasis in squamous cell carcinoma

- **201-Patient Non-Small Cell Lung Cancer Study:** In its first clinical study, MenaCalc Lung was used to evaluate 201 patients with (mostly early stage) non-small cell lung cancer (NSCLC). The data, which were presented in April 2015 in a poster session at the American Association for Cancer Research annual meeting, showed;
  - Mena^{calc} Lung scores were significant higher (p=0.001) in patients with squamous cell carcinoma (n=32) compared to other NSCLC subtypes
  - There was no significant difference in Mena^{calc} Lung scores by sex, age or cancer stage
  - High Mena^{calc} Lung scores were associated with (at 10% significance level) decreased survival in all patients (95% C.I., p=0.08)
  - High Mena^{calc} Lung scores were significantly associated with survival in the squamous cell carcinoma (SCC) subgroup (95% C.I., p=0.04)

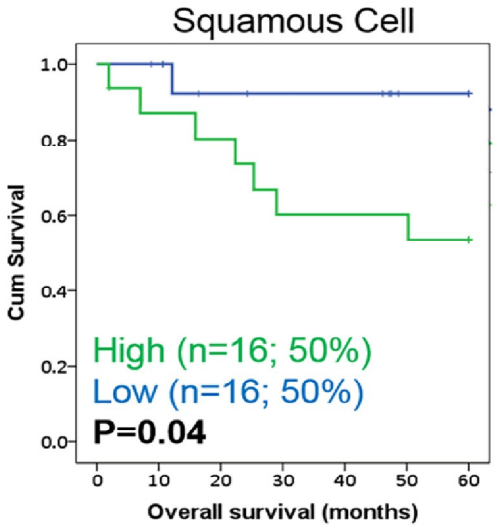
[13] Forse C. et al. *Mena^{calc} , a Quantitative Method of Metastasis Assessment, as a Prognostic Marker for Axillary Node-Negative Breast Cancer*. BMC Cancer (2015) 15:483

- There was no difference in survival based on stage of the disease
- Mena^{calc} Lung scores were twice as high in metastatic patients (note, however that this group, at just 9 patients, was very small)

Mena^{Calc} Higher in SCC



Mena^{Calc} Significantly Predicts 5-Yr Survival in SCC



SOURCE: Footnote[14]

Planned Clinical Studies:

MTST has three studies which they expect to initiate this year including two studies designed to validate the positive results demonstrated in already completed breast cancer trials as well as a chemotherapy-predictive study.

- **Kaiser cohort MetaSite/MenaCalc combined: topline data expected Q1 2016**
  - Define product specs and risk cut-points for combined MetaSite/MenaCalc score as compared to MetaSite score and/or MenaCalc score
  - Define the assay or assays to be used in subsequent validation studies
  - Primary endpoint is direct assoc. between risk of distant metastasis and MetaSite/MenaCalc score in ER+/HER2-, triple negative and/or HER2+ invasive breast cancer patients

- **ECOG 2197 cohort validation study: topline data expected Q1 2016. This is the pivotal clinical validation study for MetaStat in early stage breast cancer**
  - Compare MetaSite/MenaCalc scores with Oncotype DX's "recurrence score"
  - Primary endpoint is direct assoc. between risk of distant metastasis and MetaSite/MenaCalc score in ER+/HER2-, triple negative and/or HER2+ invasive breast cancer patients

- **Chemo-predictive study: topline data expected Q2 2016**
  - Evaluate ability of MenaCal/MetaSite Breast to predict response of adding adjuvant chemotherapy to hormonal therapy in ER+ patients
  - Primary endpoint is direct association between risk classification and benefit from chemotherapy comparing Kaplan-Meier survival curves of treatment with tamoxifen alone versus treatment with combo of tamoxifen and adjuvant chemotherapy for all patients and high, medium and low risk cohorts

[14] Gustavson, M. et al. *Mena^{Calc} as an independent prognostic factor and predictor of metastasis in Non-Small Cell Lung Cancer.* MetaStat Poster Presentation at AACR April 2015

PRESS PUBLICATIONS: Compelling Trial Data Has Attracted Several Recent Articles from Major News Outlets

The recent positive clinical trial data has sparked the attention of some major mainstream and industry-related news organizations. While we normally do not consider press coverage meaningful in terms of influence to the fundamental value or investment attractiveness of a company, we think this time warrants mention given the quality and amount of coverage (relatively tiny) MTST has received and the potential that this helps facilitate investor awareness (which can be a meaningful benefit for largely unknown microcap companies). We include some highlights below;

Medical Device Daily: August 2014 article by Medical Device Daily, a daily publication of high-tech medical technology.



MedCity News: September 2014 article by MedCity News, online healthcare news organization



Drug Discovery News: November 2014 article in DDNews, a monthly newspaper focused on biotech and pharma industries



Medscape: December 2015 article in Medscape, a WebMD publication focused on healthcare professionals



Medgadget: December 2014 article in Medgadget, an online healthcare publication written by medical doctors and biomedical professionals



Boston Business Journal: February 2015 article in Boston Business Journal, a publication with over 13M readers



GenomeWeb: February 2015 article by GenomeWeb, a NYC-based online life-sciences news organization.



The Pathologist: Feature story in the April 15th 2015 issue of The Pathologist, an online and print news organization focused on a wide range of pathology topics aimed at the professional pathologist audience



PharmaVoice.com: May 2015 article on PharmaVoice.com, an online healthcare news site aimed at life-sciences professionals



MARKETS

MTST's initial market is expected to be breast cancer, which they think will be followed with the launch of one new product every 12 - 18 months in other cancer types. After MetaSite Breast / MenaCalc Breast they hope to introduce MenaCalc Lung, MenaCalc Prostate and then MenaCalc Colorectal, which combined, MTST believes represents a total addressable U.S. patient population of approximately 560k (or ~$644M).

We calculate total economic market size by multiplying estimated addressable patient population sizes by average expected price per test. We note that test pricing is currently unknown and will likely be, at least initially, influenced by reimbursement as well as potentially by pricing of competitors' tests. MTST has calculated what they believe is a reasonable expectation of initial pricing (which we detail later) of approximately $1.0k - $1.4k per test. This is well below the price of competitors' offerings. We think with adoption, growing demand and favorable reimbursement, average price per test could increase and, potentially, significant so.

The aggregate U.S. market size as well as what MTST has calculated as their addressable domestic market for each product is in the table below.

	2014 U.S. Incidence	Deaths	Addressable Patient Population
Total Cancer	**1,665,540**	**585,720**	**559,712**
Epithelial Cancer	**1,469,710**	**515,434**	**559,712**
Breast Cancer	232,670	40,000	186,136
Lung Cancer	224,210	159,260	114,347
Prostate Cancer	233,000	29,480	209,970
Colorectal Cancer	136,830	50,310	49,259

SOURCE: National Cancer Institute, American Cancer Society, MetaStat Inc.

- **Breast cancer:** Clinical data has shown a statistically significant association between MetaSite Breast scores and risk of metastasis in women with ER-positive/HER2-negative breast cancer. This represents approximately 60% of all breast cancer cases, or an annually diagnosed U.S. population of about 140k people. MTST believes there may be an even lower-hanging fruit opportunity within this 140k person segment. Those being the 40%-45% of ER-positive/HER2-negative breast cancers which are diagnosed as "intermediate" risk by Genome Science's Oncotype DX test (we cover this topic further in the next section). MTST believes an "intermediate" risk result provides no "actionable" information and, therefore, this patient market (equal to 140k x 45% = **63k**) could be a particularly receptive market for MTST's tests.

  Clinical data has shown a statistically significant association between high MenaCalc scores and risk of cancer death in node-positive/ER-negative breast cancer as well as risk of all-cause death in axillary node-negative breast cancer. MTST believes these patient populations are not being addressed by currently available gene panel tests (such as Oncotype DX) and estimates this market at approximately 46k people.

  So, in aggregate, MTST believes their addressable U.S. market is approximately 140k (MetaSite Breast/MenaCalc) + 46k MenaCalc = **186k** people (~$214M), with a potential particularly receptive market of **63k** (~$73M).

- **Lung cancer:** The recently presented clinical data from the 201-patient NSCLC study showed a statistically significant association between high Mena^{calc} Lung scores and survival in squamous cell lung cancer patients. In addition, Mena^{calc} Lung scores were twice as high in metastatic NSCLC patients. NSCLC represents approximately 85% of all lung cancer cases, or an annually diagnosed U.S. population of about 191k people. Excluding the ~40% of NSCLC patients which are diagnosed at stage IV, leaves an estimated U.S. addressable population of about **114k** people (~$131M). We also note that approximately 30% of NSCL cancers are squamous cell, which possibly could eventually present to be a low-hanging fruit opportunity - this approximates to a domestic population of **34k** people (~$39M).

- **Prostate cancer:** Prostate cancer has one of the highest rates of survivability of all cancers with only about 13% of people diagnosed eventually dying of the disease. And 5-year survival is 99.2% - the highest among all cancers. It is also the most frequent cancer in men. We think prostate cancer, due to the relatively high prevalence, lack of effective diagnoses and massive overtreatment of the disease, could be a particularly attractive market for MTST. In addition, prostate cancer, unlike most cancers, may lend itself to individuals being tested multiple times per year.

  The current standard screening method is prostate-specific antigen (PSA) test, which while used almost 23M times each year in the U.S., has been widely criticized as ineffective at determining risk of dying of the disease. In fact, in a well-publicized announcement, based on the results of several large clinical trials in the U.S. and Europe, in 2012 the U.S. Preventative Services Task Force (USPSTF) recommended that healthy men without any symptoms of prostate cancer not receive a PSA test. The chairwoman of the task force noted that, "Unfortunately, the evidence now shows that this test does not save men's lives. This test cannot tell the difference between cancers that will and will not affect a man during his natural lifetime. We need to find one that does." The task force gave the PSA test its lowest rating, D, noting that it does more harm than good.

  Assuming clinical data supports an association between MenaCalc scores and risk of dying of prostate cancer, a Mena^{calc} Prostate test could potentially be "the" test that the USPSTF hopes to find that will save men's lives. A study published in the New England Journal of Medicine in 2012 showed no difference in survival of prostate cancer patients in those that underwent surgery versus those that underwent "watchful waiting" (i.e. were just closely monitored) - indicating that, in general, prostate cancer treatment may have no survival benefit. Annually, approximately 240k men are diagnosed with prostate cancer and about 1M men will undergo biopsies

related to diagnosis of the disease. Of those patients diagnosed, only about 3% are at risk of progression yet almost one-half are treated with surgery or radiation. Those that undergo treatment are at risk for significant lifelong side effects including incontinence and sexual dysfunction.

MTST calculates the addressable U.S. prostate cancer population as the 90% of diagnosed patients (almost all of which will not die of the disease) that are potentially eligible to receive treatment - which represents an addressable U.S. market of **210k (**~$242M or almost $725M if used 3x per year). MTST also envisions, that unlike their other tests, a Mena^{calc} Prostate test could be used several times per year (an average of three times per year) as patients undergo watchful waiting.

- **Colorectal cancer:** MTST views those colorectal cancer patients diagnosed with stage II and III of the disease as their target market for a Mena^{calc} Colorectal cancer test as it remains unclear, based on the totality of clinical studies, whether these groups benefit from chemotherapy. This U.S. population is about **49k** people (~$56M).

COMPETITION

If eventually commercialized, MTST's breast cancer assays will not be the first or only metastatic risk-based cancer diagnostics on the market and will compete with Genomic Health's Oncotype DX as well as MammaPrint (Agendia), Prosigna (NanoString) and IHC4 (Genoptix/Novartis). Initially, the company expects to address medical need breast cancer segments that are not fully served by commercially available products. MTST believes their technology can compete with these already established products based on their appropriateness for a larger portion of breast cancer sub-types and providing more "actionable information".

The three competing tests are very similar to one another in that they are all gene-based diagnostic panels that measure up-regulated genes associated with growth and proliferation of the primary tumor. MTST believes these genes are surrogate markers at best and lack the precision associated with the "drivers" of the metastatic cascade. All three competing products are based on the same technological premise and have similar methodologies - with the main differences between these tests being the number of genes that they test for.

Oncotype DX is by far the current market leader with almost 100k breast cancer tests ordered annually and generating close to $300M of revenue for Genomic Health. As such, and due the similarity amongst the gene panel assays (including the cancer subtypes for which they are appropriate), we will limit our competition discussion solely to Oncotype DX. Relevant background of Oncotype DX includes;

- initially launched in January 2004 for early stage invasive breast cancer
- supported by clinical data from over 9k patients and six validation studies
- appropriate only for ER-positive, HER2-negative
- for use in assessing likelihood of distant breast cancer as well as to predict the benefit of adjuvant therapy
- marketing materials note that studies have shown use of Oncotype DX Recurrence Score (prediction of adjuvant therapy benefit and likelihood of 10-year distant recurrence) results in changing of treatment decisions 30% of the time
- test results are "high", "intermediate" or "low" risk of cancer recurrence
- included in major clinical guidelines for chemotherapy decision making
- average per test selling price of ~$3.4k (although this may fall to ~$2.9k based on a proposed change to Medicare reimbursement rate)
- while the majority of Genomic Health's revenues continue to come from the breast cancer test, since the initial launch in 2004 the company has introduced other tests including;
  - Jan 2010: colon cancer (Stage II) test
  - Dec 2011: local recurrence of pre-invasive (ductal carcinoma in situ) breast cancer test
  - June 2012: colon cancer (Stage III) treated with oxiliplatin adjuvant therapy
  - May 2013: prostate cancer test for men at low risk

Competitiveness of MetaSite's Tests:
MetaStat believes their technology provides certain benefits as compared to Oncotype DX, affording them the ability to effectively compete with the market leader and other metastatic risk-based diagnostics. These benefits include;

- **Greater "actionability":** similar to MetaSite Breast, Oncotype DX stratifies results as patients being at high, intermediate or low risk of metastasis/cancer recurrence. However, based on clinical studies, Oncotype DX

produces, on average, an intermediate risk result approximately 35% - 45% of the time. This compares to only about 27% of the time for MetaSite Breast. As an intermediate risk result is essentially inconclusive in order to use to make treatment decisions, the proportionally fewer of this result the more useful the test will be for physicians and patients. Upcoming study data could potentially show that by combining MetaSite and MenaCalc together that this already relatively small 27% intermediate risk cohort can be narrowed even further

- **Superior performance to IHC4/Oncotype DX:** results of the 481-patient study published in August 2014 in JNCI showed MetaSite Breast scores were more strongly correlated with metastatic risk than were IHC4/Oncotype DX scores. In addition, MetaSite score was only weakly correlated with IHC4 (i.e. - indicating MetaSite score provides additional actionable information)
- **Metastatic process vs. Gene Signature:** all the competing products are gene signature tests which provide information only about the properties of the primary tumor itself. This contrasts with MetaSite's tests which provide more functional information specific to the metastatic process and tumor microenvironment.
- **Cancer subtypes:** MenaCalc may be appropriate for HER2-positive and triple-negative breast cancers (additional validation necessary) which would expand MTST's target market to all breast cancer subtypes. This could be a significant advantage to competitor's tests which are only appropriate for ER-positive/HER2-negative
- **Pricing:** As noted earlier, while ultimate pricing of MTST's tests is an unknown, and which may be influenced by reimbursement as well as demand, the company has noted that they expect to introduce their breast cancer tests at about $1.0k - $1.4k. This is well below competitor offerings which range from $2k to $4k per test.

Upcoming Studies Should Provide Further Insight

Three more major breast cancer studies are planned or already ongoing which should provide further insight into the performance and utility of the technology, including additional information about how well MTST's tests stack up against the current market leading metastatic-risk based breast cancer test, Oncotype DX. If positive, these studies will provide further clinical support for the launch of MenaCalc/MetaSite Breast. As a reminder these studies are;

- Kaiser Validation Study: ~500-patient study to replicate findings of the 481-patient, JNCI-published study which showed MetaSite was predictive of distant metastasis and outperformed IHC4 (which is sometimes used as a surrogate for Oncotype DX). This clinical study will also evaluate MetaSite and MenaCalc together using a combined algorithm in patients with all breast cancer subtypes. Top-line results are expected in Q1 2016.
- ECOG 2197 Validation Study: powered to assess MenaCalc/MetaSite ability to predict survival independent of chemotherapy treatment in all breast cancer subtypes (including HER2-positive and triple negative). Results of this study could be particularly insightful as it will be the first treatment-related study and will compare performance in the treatment/no-treatment cohorts to Oncotype DX. Positive results could be a significant "win" for MTST, particularly if they are positive in all subtypes as Oncotype DX is inappropriate for HER2-positive and triple negative patients. Top line data is expected in Q1 2016.
- Chemo-predictive: also expected to initiate later this year. Oncotype DX is used by physicians to make treatment decisions. This chemo-predictive study should provide information of the utility of MTST's tests to do the same. Top line data expected in Q2 2016.

    - Noteworthy are results of Genomic Health's **T**rial **A**ssigning **I**ndividua**L**ized **O**ptions for treatment (**Rx**), or TAILORx, trial. The study, which includes over 10k patients with node-negative, ER+/HER2- breast cancer, is assessing whether GHDX's OncoType DX assay can effectively stratify which cases will and will not respond to chemotherapy. Of the 10k plus patients, 16% had a low OncotypeDX recurrence score and were treated with only hormone therapy, 67% had an intermediate score and were randomized to either chemo or hormone therapy and 17% had a high score and were treated with both chemo and hormone therapy. The findings, presented at the European Cancer Congress in late September, found that 99.3% of patients with a low OncotypeDX recurrence score (and therefore were not treated with chemo) were disease-free after five years.

      Given the significant physical and emotional side effects (as well as cost) of chemotherapy, being able to effectively identify those patients which can skip chemo is of high value to both practitioners and patients. While OncotypeDX appears to be able to stratify at least a portion of the patients, it's important to note that 67% (or 2 of 3) patients had an intermediate score which provides no actionable information (i.e. "will or will they not respond to chemo?").

      MTST's technology, in already completed clinical trials, has demonstrated an "intermediate risk" grouping of approximately 27% (i.e. – much better than OncotypeDX's). While these have not been chemo-predictive

studies, these results may bode well for MetaSite/MenaCalc Breast providing a tighter range of intermediate risk patients, therefore offering a diagnostic that would have utility for a greater portion of the ER+/HER2- breast cancer population and clinicians more actionable information. MTST's chemo-predictive study (summarized above) should provide much greater insight into how MetaSite/MenaCalc breast stacks up against OncotypeDX in this indication.

COMMERCIALIZATION

MetaStat has outlined an initial commercialization strategy that they believe will minimize risk of early failure, keep costs down and provide the quickest time-to-market. This includes commercializing their assays as laboratory developed tests (LDTs) instead of seeking formal FDA clearance and processing the tests in-house at a CLIA certified lab (certification of which they expect to have completed in calendar Q1 2015) at their Boston location. Importantly, in Septmeber MTST received Massachusetts state licensure of their lab. This is the last major step before receiving CLIA certification from CMS. The breast cancer tests are expected to be the first to launch followed by tests for lung, prostate and colorectal cancers.

LDT Route
The LDT route has been very popular and followed by a substantial number of diagnostic companies (including Genomic Health with Oncotype DX) with over 11k LDTs currently commercialized in the U.S. by more than 200 labs. The LDT route has advantages and disadvantages. The main advantage is that it does not require obtaining FDA clearance (510k or PMA), a process which can be time-consuming and costly. There is also no guarantee that FDA will approve/clear the tests for marketing and even if they do, that the full breadth of product claims sought will be allowed. The disadvantages are LDTs can only be processed in the lab where they were developed - which precludes the direct sale to or processing by other labs, and lack of FDA clearance may be perceived as less-validated.

And there is a relatively new risk related to LDTs - that being that while FDA has had discretion in regulating these tests (which they have historically decided not to do), the agency recently issued a guidance document which proposes a risk-based oversight framework for LDTs. This oversight is expected to include premarket review for what the agency will classify as higher-risk tests that compete against already FDA-approved companion diagnostics and a potential phase-in over time of premarket review for other high risk and moderate risk LDTs. The premarket review phase-in period could be as long as five years, if it applies at all, and may require the manufacturer to validate performance claims with clinical data. While oversight of LDTs may never happen, MTST has noted that they are progressing in a fashion where they hope to be able to meet the requirements if necessary. This includes further validation of their tests with rigorously-designed clinical studies that they believe will meet submission quality standards. It is our opinion that FDA may treat LDT oversight with kid gloves, at least over the near-term, given that stringent clearance requirements could have the effect of potentially decimating this hugely important cog in the medical diagnostics space.

Outsource Sales Process
Keeping with the theme of low-risk and minimal upfront cost, MTST expects (at least initially) to sell their tests through contract sales organizations and/or strategic distribution and commercialization partners. They plan to engage already established sales organizations with existing sales and marketing infrastructure targeting the cancer diagnostic space. This avoids the cost and time to hire and train an internal sales force and, while maybe not providing the same amount of operational leverage that a direct sales strategy might, outsourcing should require fewer resources to manage and mitigates financial risk, in the event sales underperform. MTST may in the future supplement third-party sales by hiring an internal sales force.

Reimbursement
MTST expects MetaSite Breast and MenaCalc to be initially reimbursed under existing CPT code 88361: *Morphometric analysis, tumor immunohistochemistry (e.g. HER2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, each antibody, using computer assisted technology*. Since MTST's lab will both prepare the sample and interpret the result, the company believes they will be eligible for reimbursement of both the technical and professional component. CMS reimburses CPT 88361 $109 for the technical component and $60 for the professional component. And since their tests use a triple stain, requiring preparation and reading the sample for each stain, MTST believes they will be able to bill CPT 88361 five times for each MetaSite/MenaCalc and three times for each MenaCalc test processed.

Private payers typically follow CMS' lead and will reimburse when there is an established CPT code. In general, private payers reimburse at about 150% the rate of CMS, which would be approximately $1,268 for the combination MetaSite/MenaCalc tests.

MetaStat calculates an average expected reimbursement rate for the breast cancer indication based on the weighted average of three likely reimbursement scenarios and an estimated public and private payer mix of 28% of total reimbursement coming from Medicare/Medicaid and 72% coming from private payers. Using this weighted average and calculated public/private payor mix, the company believes they can expect an average reimbursement of about $1,364/test for the combined MetaSite/MenaCalc test for breast cancer and $1,065 for the MetaSite Breast test or the MenCalc™ test.

In addition, the company may elect to submit for reimbursement under a non-specific miscellaneous CPT code, reimbursement amounts which are set by local Medicare contractors and payment approval of which is reviewed on a case by case basis. Although reimbursement may be greater per test, the collections process is more arduous, resource intensive, costly, and time consuming.

In the future MTST may consider applying for a CPT code unique to their tests. While this could provide for greater reimbursement amounts, it likely would be a several-year endeavor that is usually initiated after product launch. CMS might require MTST to demonstrate that their tests are not only accurate and, potentially higher performing than other metastatic risk tests, but also that they improve patient outcomes, reduce healthcare costs or otherwise change clinical practice for the better.

VALUATION / RECOMMENDATION

Ballparking initial launch in mid/late calendar 2016…
MTST has indicated that they hope to have their initial breast assay(s) commercialized in the U.S. market sometime in calendar 2016 with the launch and roll-out supported by the existing positive clinical data as well as more data from the newly initiated studies. Prerequisite for the launch will be completing any necessary build-out and regulatory/accreditation requirements of their lab in order to meet CLIA compliance. With Massachusetts state licensure and CLIA certification already attained, the regulatory hurdles have already been cleared. The company will also need to line up initial distribution/sales infrastructure and will also be looking to raise additional capital to fund ongoing operations including R&D/clinical trial activities as well as any pre-launch preparations.

Given the list of boxes that need to be checked off prior to initiating launch, we are modeling initial introduction of the breast cancer assays around mid-to-late calendar 2016. MTST hopes to establish substantial distribution reach at the outset by partnering with well-established sales organizations and through relationship-building at the hospital and cancer center levels. We model approximately $1.5 million of revenue in fiscal 2017 (ending Feb 28, 2017), which represents about 2% of the low-hanging fruit addressable breast cancer market (i.e. - Oncotype DX "intermediate risk" market) and less than 1% of the total addressable breast cancer market.

Market share gains from low-hanging fruit, expanded label…
The second and third years on the market (fiscal 2018 and 2019) we model revenue of approximately $5.9M and $21.5M, which assumes deeper penetration of the (previously defined) low-hanging fruit opportunity but represents less than 9% penetration of the total addressable market in 2019. This compares to the $4.8M and $27M Oncotype DX generated in its second and third full years after launch. We further assume MTST realizes average pricing of about $1.1k per test, a significant discount (i.e. again, applying conservative assumptions) to Oncotype DX's ~$2.9k - $3.5k).

We think our somewhat more conservative approach is warranted given the relative dearth of competition to Oncotype DX following its launch in 2004 and the fact that Genomic Health had substantially more financial resources at the time (compared to MTST today) to support the roll-out. However, we also think MenaCalc/MetaSite Breast have the potential to be well received given the compelling clinical data to-date (which indicates potentially superior performance over Oncotype DX) as well as near-term data which could provide further insight into the utility of the technology and potentially demonstrate even greater benefit over Oncotype DX (possibly including in cancer subtypes which exclude competing tests).

MTST has indicated that they will continue to build their clinical database beyond the already planned studies and look to further broaden the indicated uses for the breast cancer assays (similar to what GHDX did with Oncotype DX following initial commercialization). We think an expanded breast cancer label, which could include additional cancer subtypes, survival independent of therapy and predictive of chemotherapy response (among others) would provide meaningful additional competitive benefits and could result in an acceleration in market share gains.

Follow-on launches in other cancers…

Following launch in breast cancer MTST hopes to bring one new assay to market in other cancers at a rate of one every 12 to 18 months. And while we think the bulk of the revenue opportunity lies with breast cancer, expanding the portfolio to include additional cancers offers meaningful market-expansion and scalability opportunities.

The positive clinical data presented in non-small cell lung cancer at AACR in April 2015 was the first major step towards commercialization of a lung cancer test, which is expected to be MTST's next product launch in the U.S. We currently model this to be a fiscal 2018 event. Importantly, while GHDX has Oncotype DX tests for cancers of the breast, prostate and colon, they do not for lung cancer. In addition, the Mena^{calc} Lung data demonstrated significant predictive ability in squamous cell. The lack of significant competition and the presence of a low-hanging fruit opportunity in SCC may present ripe conditions for a particularly receptive market for MetaStat's lung cancer assay.

Beyond lung cancer, visibility of the potential timing of introduction of tests in prostate and colorectal cancers is somewhat more cloudy, particularly given the lack of clinical data to be able to anchor to. However, as demonstrated in breast and lung cancer, patient samples have been readily available and these studies can be completed fairly swiftly and cost-effectively. In the span of just over 3 years GHDX was able to bring three new tests to market. As such, we think it is reasonable MTST could have lung, prostate and colorectal cancer tests commercialized within the next five years, and potentially earlier (MTST is aiming for closer to 3 - 4 years). We more conservatively model launch of a prostate and colorectal cancer test in fiscal 2020 and 2021, respectively.

Value MTST at $11/share

We value MTST using a combination of 10-year DCF and P/S comparables. We model incremental revenue contribution to begin for tests in; NSCLC in 2018, prostate cancer in 2020 and colorectal cancer in 2021. However, the breast cancer assays remain the majority driver of revenue throughout the term of 10-year DCF. We model revenue to grow from $21.5M in 2019 to approximately $111M in 2025 (the ninth year on the market). For reference, GHDX generated almost $260M in revenue from their Oncotype DX franchise (the majority of which comes from their breast cancer assays) 9 years post-launch - which arguably indicates our model is conservative.

We assume gross margin grows from about 41% in the initial year of launch with relatively low production volumes to around 80% with improvement in reimbursement and laboratory/operating efficiencies. For reference, Oncotype DX gross margins are currently about 82%.

Using these inputs along with a 10% discount rate and 2% terminal growth rate, our 10-year DCF calculates fair value at approximately **$11/share**.

This valuation is largely supported with P/S comparables. Competitors NSTG and GHDX trade at 4.5x and 3.5x 2015 analysts' consensus revenue estimates, respectively. Applying the average (4.0x) to our estimated 2018 revenue of $5.9M and discount this back at 15%, which results in a per share value of approximately $10.

FINANCIAL MODEL

MetaStat, Inc.

	2015 A	Q1 A	Q2 A	Q3 A	Q4 E	2016 E	2017 E	2018 E	2019 E
Breast Cancer									
Addressable market penetration	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.68%	2.38%	8.71%
Revenue	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$1,467.3**	**$5,136.0**	**$18,910.8**
NSCLC									
Addressable market penetration	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.69%	2.36%
Revenue	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.0**	**$756.8**	**$2,551.6**
Prostate Cancer									
Addressable market penetration	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Revenue	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.0**	**$0.0**	**$0.0**
Colorectal Cancer									
Addressable market penetration	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Revenue	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.0**	**$0.0**	**$0.0**
Total Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1,467.3	$5,892.8	$21,462.5
YOY Growth	-	-	-	-	-	-	-	*301.6%*	*264.2%*
Cost of Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$865.7	$2,710.7	$7,082.6
Gross Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$601.6	$3,182.1	$14,379.9
Gross Margin	-	-	-	-	-	-	*41.0%*	*54.0%*	*67.0%*
SG&A	$3,524.9	$948.9	$1,076.0	$656.9	$1,115.0	$3,796.9	$5,167.8	$7,041.8	$14,959.4
%SG&A	-	-	-	-	-	-	*352.2%*	*119.5%*	*69.7%*
R&D	$1,266.2	$219.3	$318.0	$405.9	$712.0	$1,655.2	$3,851.0	$4,044.0	$4,417.0
%R&D	-	-	-	-	-	-	*262.5%*	*68.6%*	*20.6%*
Operating Income	($4,791.1)	($1,168.2)	($1,394.0)	($1,062.8)	($1,827.0)	($5,452.1)	($8,417.2)	($7,903.8)	($4,996.5)
Operating Margin	-	-	-	-	-	-	*-573.7%*	*-134.1%*	*-23.3%*
Total Other (Inc) / Exp	$3,204.4	($93.3)	($132.1)	$173.4	$83.0	$193.2	$425.0	$81.0	$207.0
Pre-Tax Income	($7,995.5)	($1,074.9)	($1,261.9)	($1,236.3)	($1,910.0)	($5,645.3)	($8,842.2)	($7,984.8)	($5,203.5)
Taxes	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($8,237.5)	($2,197.7)	($1,331.1)	($1,306.9)	($1,992.0)	($6,989.8)	($8,842.2)	($7,984.8)	($5,203.5)
YOY Growth	*53.5%*	*78.4%*	*-69.1%*	*-7.2%*	*146.0%*	*-15.1%*	*26.5%*	*-9.7%*	*-34.8%*
Net Margin	-	-	-	-	-	-	*-602.6%*	*-135.5%*	*-24.2%*
EPS	($4.96)	($1.21)	($0.73)	($0.72)	($1.08)	($3.83)	($2.65)	($1.79)	($1.05)
YOY Growth	*30.4%*	*42.1%*	*-71.1%*	*-9.3%*	*129.2%*	*-22.8%*	*-30.8%*	*-32.5%*	*-41.0%*
Diluted Shares O/S	1,662	1,809	1,823	1,821	1,850	1,826	3,340	4,471	4,940

Brian Marckx, CFA

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LEADERSHIP

Management

Douglas A. Hamilton, BSc., MBA
President and Chief Executive Officer
Mr. Hamilton was elected President and Chief Executive Officer in June 2015 after consulting for the company as acting Chief Financial Officer since August 2014. Mr. Hamilton has over 20 years experience in the life-sciences industry with broad domain expertise including financial management, management consulting, venture capital, and R&D operations management. Prior to joining MetaStat, Mr. Hamilton served as Partner at New Biology Ventures since 2007 and CFO of SEA Medical Systems, a Silicon Valley health-tech company from 2012 to 2014. From 1999 to 2006, Mr. Hamilton served as COO and CFO for Javelin Pharmaceuticals (purchased by Hospira), a commercial stage pharmaceutical company focused on the development and commercialization of a portfolio of acute pain medications. While at Javelin, Mr. Hamilton led the company to commercialization and through its successful national markets up-lisitng. Prior to Javelin, Mr. Hamilton was the CFO and Director of Business Development for PolaRx Biopharmaceuticals, Inc. At PolaRx he helped developed the orphan drug Trisenox® and co-led the $45.2 million merger with Cell Therapeutics (owned by Teva Pharmaceuticals). Mr. Hamilton also worked at Pfizer and Amgen in project management and portfolio management roles including serving as Project Manager for the Vfend® and Zithromax® product teams at Pfizer and Aranesp®, Epogen®, Stemgen®, MGDF, and Cell Therapy product development teams at Amgen. Prior to Amgen, Mr. Hamilton served in the sales and marketing group at Pharmacia Biotech (now GE Healthcare Life Sciences), and in the recombinant DNA vaccine research group at Connaught Laboratories (now Sanofi-Pasteur). Mr. Hamilton earned his honors Bachelor of Science degree from the Department of Medical Genetics at the University of Toronto and his MBA from the Ivey Business School at Western University.

Michael J. Donovan, PhD, MD
Chief Medical Officer
Dr. Donovan joined the company as acting chief medical officer in August 2015. Dr. Donovan is board-certified in anatomic and clinical pathology and pediatric pathology with extensive experience in designing and implementing clinical studies. He has spearheaded the utilization of multiplex tissue and fluid-based assays and coupled mathematic applications to produce clinically relevant diagnostic/predictive/prognostic outcome models for a variety of tumor types and disease states. Dr. Donovan also serves as a Professor of Experimental Pathology and Director of the Biorepository and Pathology core at the Icahn School of Medicine at Mt. Sinai, New York City, New York. In addition to an academic career at Harvard Medical School and Boston Children′s Hospital, Dr. Donovan has over 20 years′ experience in the biotechnology industry, serving in various senior management roles at Millennium Pharmaceuticals and Incyte Pharmaceuticals. He most recently served as Chief Medical Officer of Exosome Diagnostics, Inc. and Chief Scientific Officer for Aureon Biosciences Corporation. Dr. Donovan graduated from Rutgers University with a BS in zoology, a MS in endocrinology and a PhD in cell and developmental biology. He received his MD from the University of Medicine and Dentistry of New Jersey.

Mark Gustavson, Ph.D.
Vice Presiden of Diagnostics
Dr. Gustavson joined the company as Vice President of Diagnostics in August 2014. Dr. Gustavson has more than 10 years of experience in translational oncology, biomarker and diagnostics development, and quantitative pathology. Prior to joining the company, Dr. Gustavson was a Consultant for Oncology Biomarker Development at Genoptix Medical Laboratory. From 2006 to 2012, Dr. Gustavson was with HistoRx, Inc. where he played a central role in the development and commercialization of the quantitative pathology platform, AQUA® Technology. With HistoRx, Dr. Gustavson served as Director of Operations where he oversaw assay and platform development as well as clinical validation of the breast cancer diagnostic test, IHC4. Dr. Gustavson did his post-doctoral fellowship at Yale University and received his Ph.D. in Cancer Biology from Vanderbilt University School of Medicine. Dr. Gustavson has over 40 peer-review publications and abstracts, and 9 patents.

Daniel H. Schneiderman
Vice President of Finance & Secretary
Daniel H. Schneiderman was appointed Vice President of Finance effective December 21, 2012 and has served as the Company's Vice President and Comptroller since February 27, 2012. Mr. Schneiderman has ten years of investment banking and corporate finance experience, focusing on private and public equity for small and mid-market capitalization companies mainly in the healthcare and life sciences sectors. Prior to joining the Company, 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.

Heiner Dreismann, Ph.D.
Diagnostic Consultant
Dr. Dreismann joined the company as a consultant (head of diagnostics) in October 2013. Dr. Dreismann is a seasoned executive with more than 24 years of experience in the health care industry, and is regarded as a pioneer in the early adoption of the polymerase chain reaction (PCR) technique, one of the most ubiquitous technologies in molecular biology and genetics research today. Dr. Dreismann had a successful career at the Roche Group from 1985 to 2006 where he held several senior positions, including President and CEO of Roche Molecular Systems, Head of Global Business Development for Roche Diagnostics and Member of Roche's Global Diagnostic Executive Committee. Dr. Dreismann currently serves on the boards of several public and private health care companies. He earned a master of science degree in biology and his doctor of

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philosophy degree in microbiology/molecular biology (summa cum laude) from Westfaelische Wilhelms University (The University of Münster) in Germany.

Board of Directors

Richard J. Berman

Richard J. Berman's business career spans over 35 years of venture capital, senior management and merger and acquisitions experience. In the past 5 years, Mr. Berman has served as a director and/or officer of over a dozen public and private companies. From 2006 to 2011, he was Chairman of National Investment Managers, a company with $12 billion in pension administration assets. From 2008 to 2010, Mr. Berman was Chairman and CEO of NexMed Inc., a public biotech company. From 1998 to 2012, Mr. Berman served as a Director of Easy Link Int'l. Mr. Berman is currently a director of three public companies: Advaxis, Inc., Neostem, Inc. (since 2005), and Lustros, Inc. (since 2012). From 1998 to 2000, he was employed by Internet Commerce Corporation (now Easy Link Int'l) as Chairman and CEO. Previously, Mr. Berman worked at Goldman Sachs; was Senior Vice President of Bankers Trust Company, where he started the M&A and Leveraged Buyout Departments; created the largest battery company in the world in the 1980s by merging Prestolite, General Battery and Exide to form Exide Technologies (XIDE); helped to create what is now Soho (NYC) by developing five buildings; and advised on over $4 billion of M&A transactions (completed over 300 deals). He is a past Director of the Stern School of Business of NYU where he obtained his B.S. and M.B.A. He also has U.S. and foreign law degrees from Boston College and The Hague Academy of International Law, respectively.

Johan M. (Thijs) Spoor

Mr. Spoor was appointed to our Board of Directors on February 27, 2012, effective as of April 7, 2012 and was appointed Chairman of the Board on December 21, 2012. Mr. Spoor is currently the CEO, President and Director of FluoroPharma Medical Inc., a public biopharmaceutical company. He has held these positions at FluoroPharma since May 2011. Previously, Mr. Spoor served as CFO for Sunstone BioSciences from February 2010 through September 2010. Prior to joining Sunstone BioSciences, he worked as a consultant at Oliver Wyman from December 2008 through February 2010 focusing on helping pharmaceutical and medical device companies evaluate their global revenue potential.

Mr. Spoor was 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 / GE Healthcare where he worked in seven countries in a variety of roles including setting up GMP facilities, accountability for the nuclear cardiology portfolio and most recently as the Director of New Product Opportunities leading the PET strategic plan.

Mr. Spoor holds a Nuclear Pharmacy degree from the University of Toronto as well as an Master of Business Administration from Columbia University with concentrations in finance and accounting. Mr. Spoor also sits on the Board of Directors of AtheroNova, Inc. (AHRO) and Protea Biosciences Group, Inc.

H. Philip Goodeve

Mr. Goodeve was appointed to our Board of Directors effective as of October 15, 2014. Mr. Goodeve has over 25 years of experience in the global capital markets and has been a corporate finance consultant since 2009. He has led over 100 change of control transactions, 10 IPOs and 15 turnarounds. Most recently, Mr. Goodeve was CFO of FINCA International Inc., one of the largest microfinance banking groups in the world, with operations in 21 countries. Mr. Goodeve served as CFO of CroMedica International Inc., one of the largest providers in the world of clinical trial management services to biotech and pharmaceutical companies, were he successfully executed a corporate turnaround and sale of the firm. Amongst other prior roles prior, Mr. Goodeve was the Global Co-Head of Financial Services Investment Banking for CIBC Capital Markets. Mr. Goodeve also currently serves as Chairman of the Board of Integral Securities in Canada, and he has served on numerous other public and private company boards. Mr. Goodeve's experience in the global capital markets provides a valuable perspective to our board of directors on strategy, competitive industry dynamics and capital markets transactions. Mr. Goodeve earned his Master of Business Administration from Harvard Business School and an Honors Bachelor of Commerce from Queen's University.

Martin J. Driscoll

Mr. Driscoll has more than 30 years of experience in the biopharmaceutical industry. Since November 2010, he has served as president and Chief Executive Officer of Asmacure Ltée, which is focused on the development of small molecule cholinergic receptor modulators for the treatment of pulmonary diseases. Previously, he was the CEO of Javelin Pharmaceuticals, a company focused on the development of acute care pain products. Mr. Driscoll led a successful M&A effort at Javelin culminating in the sale of the company to Hospira, Inc. in July 2010. Earlier in his career, he spent 18 years at Schering-Plough, where he held various global general management positions, including leadership of the company's largest division, Key Pharmaceuticals. Following his tenure at Schering-Plough, Mr. Driscoll held senior management positions at ViroPharma and Reliant Pharmaceuticals. He also co-founded Pear Tree Pharmaceuticals, a privately held developer of women's healthcare products. Mr. Driscoll holds a B.Sc. in communications from the University of Texas at Austin.

Oscar L. Bronsther, M.D., F.A.C.S.

Dr. Bronsther is a Diplomat, American Board of Surgery, and since November 2008, has served as the Chairman, Section of General Surgery, at Inova Fairfax Hospital. Since September 2003, he has also served as Clinical Professor of Surgery at George Washington University in Washington, D.C. Dr. Bronsther served as Chief Medical Officer and Chief Executive Officer of MetaStat, Inc. from 2012 to 2015. From 2005 to 2007, he served as Chairman of the Board of National Transplant Network. Dr. Bronsther received his B.A. from the University of Rochester in 1973, his 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 the 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.

HISTORICAL ZACKS RECOMMENDATIONS



DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

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