Zacks Small-Cap Research

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Rosetta Genomics (ROSG-NASDAQ)

ROSG: Collaboration represents third platform for revenue growth, Strong financials reported for 2013, growth momentum will continue in 2014 and beyond---Outperform

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	02/26/2014
Current Price (06/25/14)	$4.35
Twelve- Month Target Price	**$10.50**

OUTLOOK

Rosetta is a molecular diagnostics company focused on microRNA-based tests for cancers and other indications. The company is currently marketing four cancer assays with focus on its lead cancer origin test.

We are optimistic with its microRNA platform technologies, which serve as the basis of continued development of molecular diagnostics. Revenue should get boosted in 2014 and beyond due to focused marketing strategy. Long term pipeline will provide sustainable growth for the years to come.

Maintain Outperform rating. Our price target is $10.50.

SUMMARY DATA

52-Week High	**$6.55**
52-Week Low	**$2.39**
One-Year Return (%)	**27.94**
Beta	**-2.92**
Average Daily Volume (sh)	**112,387**
Shares Outstanding (mil)	**11**
Market Capitalization ($mil)	**$47**
Short Interest Ratio (days)	**4.99**
Institutional Ownership (%)	**N/A**
Insider Ownership (%)	**N/A**
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 2014 Estimate	**N/A**
P/E using 2015 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Value**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2012		0.05 A		0.15 A	0.20 A
2013		0.19 A		0.21 A	0.41 A
2014		0.50 E		1.00 E	1.50 E
2015					5.50 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2012		-$5.31 A		-$0.51 A	-$2.35 A
2013		-$0.68 A		-$0.69 A	-$1.37 A
2014		-$0.80 E		-$0.78 E	-$1.58 E
2015					-$1.11 E

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

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WHAT'S NEW

Collaboration Accelerates Product Development and Represents New Avenue for Revenue Growth

A new **revenue growth platform** for Rosetta is through collaboration with biotech/pharmaceutical companies to monetize its microRNA platform technologies.

In June, Rosetta Genomics entered into an agreement with **Moffitt Cancer Center** to advance the development and commercialization of Rosetta's **thyroid neoplasia assay**.

Under the agreement, Rosetta will work with Marino Leon, M.D., associate member of the Department of Anatomic Pathology at Moffitt.

An estimated 4-7 percent of the general population develops nodules in the thyroid that can be felt on examination, though fewer than 10 percent are malignant. A fine needle aspiration (FNA), a non-surgical procedure used to obtain tissue for analysis by a pathologist, is the standard technique for detecting cancer. However, interpretation of FNA samples is not always conclusive, and up to 30 percent of samples have indeterminate results.

In April, Rosetta Genomics entered into a strategic alliance with **Marina Biotech** to identify and develop microRNA-based products designed to **diagnose** and **treat** various **neuromuscular diseases** and **dystrophies**.

The Alliance is exclusive as it relates to neuromuscular diseases and dystrophies, with both Companies free to develop and collaborate outside this field both during and after the terms of the Alliance. The Companies' initial efforts are expected to be focused on Becker and Duchenne muscular dystrophies as well as myotonic dystrophy. Financial terms and other details of the agreement are not being disclosed at this time.

Under the terms of the Alliance, Rosetta will apply its industry leading microRNA discovery expertise for the identification of microRNAs involved in the various dystrophy diseases. If the microRNA is determined to be correlative to the disease, **Rosetta** may further develop the microRNA into a **diagnostic** for patient identification and stratification. If the microRNA is determined to be involved in the disease pathology and represents a potential therapeutic target, **Marina** may develop the resulting microRNA-based **therapeutic** for clinical development.

In January, Rosetta Genomics announced that it signed a **master service provider agreement** with an undisclosed major global biopharmaceutical company, under which, Rosetta will provide its microRNA profiling and other services pursuant to a collaboration in important areas of unmet medical need utilizing a novel therapeutic approach.

This agreement leverages Rosetta's microRNA biomarker platform and expertise to assist one of the world's leading biopharmaceutical companies to advance their research and development efforts on this important, novel therapeutic approach.

In addition to the company's current cancer testing services and new products from its own, internal research and development initiatives, collaborations such as these represent **third major platform** for revenue growth for the company.

Moving forward, we believe Rosetta will enter into additional similar agreements as the company seeks to monetize its leading microRNA platform and expertise.

Other Two Platforms to Drive Revenue Growth

Focus on Currently Marketed Diagnostic Products

Based on its **microRNA platform technologies**, Rosetta currently markets four cancer tests it has developed: Rosetta Cancer Origin Test™, Rosetta Lung Cancer Test™, Rosetta Kidney Cancer Test™, and Rosetta Mesothelioma Test™.

Rosetta's lead cancer test is Rosetta Cancer Origin Test, which is covered in the US by Medicare reimbursement at $3500/test. Rosetta Cancer Origin Test may be considered in-network by major payors for over 170 million lives. Rosetta is negotiating insurance coverage for their other three cancer tests.

These marketed products, especially the lead Cancer Origin Test will be the major revenue growth driver for 2014 and beyond.

Long-term Pipeline Provides Sustainable Growth

Diagnostics

In addition to the four marketed molecular cancer tests, Rosetta is also developing both tissue and body fluid based microRNA tests for other indications. Rosetta is also developing microRNA-based **therapeutics**. We believe the long term pipeline will provide sustainable growth for the company in the years to come.

Rosetta Genomics plans to launch at least one new diagnostic assay per year beginning in 2015. The company has a number of promising product candidates under development.

The first new diagnostic product the company is going to launch is the assay for **indeterminate thyroid fine need aspirate**, which is scheduled to launch at the end of **2015**.

In 2016, the company plans to launch at least one of the following cancer diagnostics: a) **Bladder cancer** assay that predicts risk of invasiveness, for which the company has done two studies that have been published; b) **ovarian cancer** assay that predicts response to platinum treatment, for which the company has done a study and has a publication; and c) **breast cancer**, which the company is currently assessing.

The third diagnostic product under development is for early diagnosis and refined risk stratification of patients following **myocardial infarction (MI).** Such a test has the potential to influence clinical management in a cost effective manner, by improving diagnosis, refining risk stratification and guiding therapy.

Heart Failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricles to fill with or eject blood. It is the most prevalent disease in the western world and its prevalence continues to rise. It is estimated that 5 million Americans are diagnosed with HF and each year there are approximately 500,000 new HF patients. Besides its high prevalence, HF is also the most expensive disease in western countries.

Rosetta Genomics has so far performed two studies. The first study was published in the European Journal of Heart Failure (Goren et. al., 2012), showing that elevated serum levels of specific microRNAs identify heart failure patients. The second one was published in Am J Cardiology (Goren et al., 2013), correlating miR-150 to atrial fibrillation in patients with chronic systolic heart failure.

The company plans to launch HF diagnostics in **2017**.

The company is also developing diagnostic candidates for **chronic kidney rejection** and **Alzheimer's** disease. Progress will be updated over the coming months.

Therapeutic Products

microRNAs are important regulators of gene and protein expression, and as such, they represent potential targets for the development of drugs. Expression studies have indicated significant changes in microRNA expression in different disease states in comparison to normal tissue. Therefore microRNAs can serve as a basis for a new class of therapeutic products.

Rosetta Genomics has demonstrated this in liver cancer, ovarian cancer and pancreatic cancer, where differential microRNAs that were shown in tissues of patients were used to find drug candidates that could inhibit those cancers through either microRNA inhibition or mimetics.

Those microRNAs served to design modified oligonucleotides with anti-sense sequences that were used in vitro in proliferation assays. If the microRNA inhibition can lead to reduction in proliferation of cancer cell lines, the anti- microRNAs with the strongest effect over cell proliferation were chosen as the drug candidates with most potential. The ability to specifically silence virtually every gene including previously non-druggable targets has made RNAi-based therapeutics a very attractive approach for treating diseases in many therapeutic areas.

Rosetta Genomics is developing a therapeutic for cytomegalovirus **(CMV) infection**.

In January 2011, Rosetta joined the **Rimonim Consortium**, which is supported by the Office of the Chief Scientist at the Ministry of Industry, Trade and Labor of the State of Israel (OCS). The purpose of the consortium is to develop RNA interference (RNAi)-based therapeutics. As a member of the consortium, Rosetta is entitled to certain grants to support its research and development activities.

We believe the long term pipeline will provide sustainable growth for the company.

Strong 2013 Financial Results, Growth Momentum Expected for 2014

On March 31, 2013, Rosetta Genomics reported financial results for the year ended December 31, 2013.

Revenues for 2013 were $405,000, an increase of 102% compared to the $201,000 of revenues recorded for the year 2012. The company recorded gross billings for 2013 of $1.1 million, which more than doubled from $490,000 in 2012.

Cost of revenues was $709,000 for 2013, up from $258,000 for 2012 primarily due to higher volume of processed samples as well as increases in personnel and infrastructure to meet current and anticipated sample volume.

Research and development expenses for 2013 were $1.7 million, compared to $1.2 million for 2012. The increase was primarily due to an increase in headcount and lab materials.

SG&A expenses for 2013 were $11.3 million, compared to $7.0 million for 2012. This increase was primarily due to the Company's ongoing investment in its U.S. commercialization efforts, as well as to increases in business development initiatives to procure collaborative and/or licensing agreements.

Operating loss for 2013 was $13.3 million ($1.37 per share), which included $847,000 of non-cash stock-compensation expense. Operating loss for 2012 was $8.3 million, including $549,000 of non-cash stock-compensation expense.

Net loss after discontinued operations for 2013 was $12.9 million or $1.34 per ordinary share on 9.6 million shares outstanding, compared with a net loss after discontinued operations for 2012 of $10.5 million or $2.35 per ordinary share on 4.4 million shares outstanding.

As of December 31, 2013, Rosetta Genomics had $24.5 million in cash and cash equivalents, restricted cash and short-term bank deposits. The Company used approximately $12 million in cash to fund operations in 2013.

We estimate that net cash requirements to fund operations in 2014 will be in the range of $14 million to $15 million. Therefore its cash balance of $24.5 million as of December 31, 2013, combined with projected revenue growth, will be sufficient to fund operations until late 2015.

We are pleased with the strong financial performance the company achieved for 2013; though it's a little lower than our estimate of $44000 for 2013. The amount of revenue was still a small number, but we believe the growth momentum will continue in 2014 and beyond. This is already evidenced by gross billings of nearly $600,000 in the first quarter of 2014.

The company's balance sheet was strong which will allow the company to focus on long term growth strategy.

Valuation Attractive

We maintain our Outperform rating on Rosetta Genomics (ROSG) shares and reiterate our 12-month price target of $10.50 per share.

Rosetta is a revenue generating, emerging molecular diagnostics biotech company focused on molecular testing of cancers and other life threatening diseases. The company develops its diagnostic products based on the unique and proprietary microRNA platform technology.

Currently Rosetta is marketing four cancer tests with focus on its lead Cancer Origin Test. This Cancer Origin Test is covered by Medicare reimbursement and other payors covering over 170 million lives. The company is negotiating for expanded coverage for the Cancer Origin Test as well as for reimbursement for its three other marketed cancer tests.

In addition to currently marketed tests, Rosetta is also developing other tissue or body fluid based molecular diagnostics using its microRNA technologies. Current focus is on the development of a test for **heart failure**. Furthermore, Rosetta is developing microRNA based therapeutics. These long term pipeline will provide sustainable growth for the company in the years to come.

Rosetta is also collaborating with pharmaceutical/biotech companies to assist these companies to develop microRNA based therapeutics. This collaboration creates the third avenue for revenue growth.

With a focused marketing strategy in place, revenue will be boosted in 2014 and beyond. Specifically, we model $1.5 million in revenue for fiscal 2014 and revenue will grow to $125 million in 2020, a tremendous compound annual growth rate (CAGR) of 123%. With accelerated revenue growth, Rosetta will become profitable in fiscal 2018 with earnings per share (EPS) of $0.32 based on total revenue of $50 million. EPS will grow to $1.31 per share in fiscal 2010 based on total revenue of $125 million, a 102% increase in the two year period.

Rosetta has a relatively strong balance sheet. Current cash is sufficient to fund operations into 2015 according to our model.

With all these in mind, we think Rosetta's shares are undervalued at current market price. Currently, Rosetta shares are trading at about $4.4 per share, which values the company at about $48 million in market cap based on 11million outstanding shares. This is apparently a huge discount compared to its

peers. As we said, Rosetta is a revenue generating diagnostics company targeting the high growth market of molecular diagnostics. The company's microRNA platform technology has broad applications targeting both diagnostics and therapeutics. We don't think the Street has recognized the potential of high revenue growth in the coming years for Rosetta.

Based on our financial model, we think a P/E multiple of 25x is appropriate for Rosetta. If we apply this P/E coupled with EPS of $1.31 in 2020, discounted at 20% for 6 years, we come up with our price target of $10.50 per share. Our price target values Rosetta at $116 million in market cap, which we think is still conservative.

Execution is the key to achieve expected growth and will have a significant impact on the share price. The fluctuation of the broader market in the US will also have impact on the company's share price in the next 6 to 12 months. In general, we think the company has a favorable risk/award profile at this time with downside risk relatively low and high upside potential.

OVERVIEW

Rosetta Genomics (ROSG) is an Israel based **molecular diagnostic company** focused on developing and commercializing molecular diagnostics for cancers and other diseases.

ROSETTA GENOMICS™
expanding personalized medicine

Rosetta's diagnostic business is based on its unique and proprietary **microRNA (miRNA)** platform technology. MicroRNAs are naturally expressed, or produced, using instructions encoded in DNA and are believed to play an important role in normal function and in various pathologies. The DNA encoding microRNAs, previously known as "junk DNA", actually contains hundreds, possibly thousands, of tiny RNA genes that encode small RNA molecules. MicroRNAs play an important role in the regulation of protein production, and hence the onset and progression of disease.

To leverage the potential of microRNAs as a novel diagnostic platform, Rosetta Genomics has developed **proprietary methods** to extract microRNAs from a wide range of **tissue and body fluid samples** and to quantify specific microRNA expression signatures, which may be used as diagnostic panels to potentially diagnose cancers, their subtypes, as well as the origin of metastases.

Rosetta Genomics has established a College of American Pathologists **(CAP) accredited**, **CLIA-certified laboratory** in Philadelphia, PA, USA, which enables the company to commercialize its miRNA-based diagnostic tests.

Rosetta Genomics is the first commercial enterprise to focus on the emerging microRNA field. The company has developed an early and strong intellectual property position related to the development and commercialization of microRNA-based diagnostics. Using its intellectual property, collaborative relationships with leading commercial enterprises and academic and medical institutions, and expertise in the field of microRNAs, Rosetta Genomics has initiated microRNA-based diagnostic programs for various cancers.

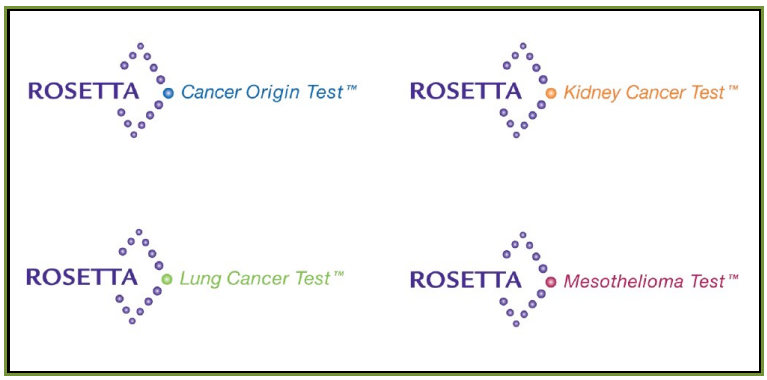
Rosetta has already developed and launched **four diagnostic tests** based on this miRNA platform:

- **Rosetta Cancer Origin Test™**: a cutting-edge molecular test that identifies the primary origin of tumors. The test is designed for cancer patients with an uncertain or unknown origin (Cancer of Unknown Primary - CUP) and other metastatic cancers where some level of uncertainty remains.

- **Rosetta Lung Cancer Test™**: a pioneering molecular test that accurately differentiates primary lung tumors. It classified neuroendocrine and non-small cell lung cancer (NSCLC); and then further subclassifies NSCLC to either squamous or non-squamous; and further subclassifies neuroendocrine to either small or carcinoid.

- **Rosetta Kidney Cancer Test™:** a novel molecular test that accurately differentiates the four main histological types of primary kidney tumors: namely, benign oncocytoma and the three most common subtypes of renal cell carcinoma (RCC): clear cell, papillary and chromophobe.

- **Rosetta Mesothelioma Test™**: the first single test that accurately differentiates malignant pleural mesothelioma from carcinomas in the lung and pleura.



The Cancer Origin Test is covered by Medicare as well as by many private insurers. The company is working with third parties to negotiate coverage of the other three cancer tests in the US.

Rosetta currently has distribution agreements with respect to some of these tests covering Australia, Canada, Greece, Romania, India, Israel, New Zealand, Qatar, Saudi Arabia, Singapore, Turkey and the United Arab Emirates. All of these distribution agreements call for samples to be sent to its CLIA-certified laboratory in Philadelphia for analysis.

In addition, Rosetta is in the **discovery stage** for a body fluid-based diagnostic test for **Heart Failure** (HF). The company has performed a proof of concept (POC) study which demonstrated that by using microRNA expression levels in serum Rosetta can identify heart failure patients. The company is currently performing additional studies involving various blood fractions to assess the feasibility to develop a minimally-invasive microRNA-based stratification test for HF.

Rosetta Genomics was founded in 2000 and is headquartered in Princeton, NJ. Its research and development center is located in Rehovot, Israel, while its CLIA lab is located in Philadelphia, PA.

INVESTMENT THESIS

Rosetta Targets the Large Medical Diagnostic Market

Rosetta Genomics is a pure play laboratory testing service provider specifically focused on high complexity, high revenue **molecular/genetics diagnostics** for cancers. Recent advances in the genomic and proteomic research, combined with the complete sequencing of the human genome, have made sophisticated new scientific testing tools to diagnose and treat diseases possible, and therefore boosted the lab testing market dramatically.

Currently, the medical diagnostic/testing market consists of three primary segments:

- Clinical Pathology (CP) lab testing,
- Anatomic Pathology (AP) testing, and
- Genetic/Molecular Diagnostic (GM) testing

CP testing is typically engaged in high volume, highly automated, lower complexity tests on easily procured specimens such as blood and urine. Clinical lab tests often involve testing of a less urgent nature such as cholesterol testing and testing associated with routine physical exams. CP testing yields relatively low average revenue per test.

AP testing involves evaluation of tissues, as in surgical pathology, or cells as in cytopathology and usually seeks to answer the question: is it cancer? The most widely performed AP procedures include the preparation and interpretation of pap smears, skin biopsies, and tissue biopsies. AP tests are typically more labor and technology intensive than clinical lab tests and have higher average revenue per test than clinical lab tests.

GM testing typically involves analyzing chromosomes, genes or DNA/RNA sequences for abnormalities. The past decade has witnessed the rapid progress in this emerging market due to the tremendous advances made in genomics and proteomics research, as well as the completion of human genome project. New tests continue to be developed at an accelerated pace in recent years, thus this segment continues to expand rapidly. Genetic and molecular testing requires highly specialized equipment and credentialed individuals (typically MD or PhD level) to certify results and typically yields the highest reimbursement levels of the three market segments.

The clinical lab testing industry consists primarily of three types of providers: hospital-based laboratories, physician office laboratories and independent clinical laboratories. The total medical testing market is a multi-billion dollar business with estimated total revenue of about $57 billion in 2010 and hospital affiliated labs account for 50% of the market share.

Rosetta Genomics is an **independent lab testing provider** and it targets the **genomic/molecular testing** segment with a focus on **cancer diagnostics.** It is estimated that the genetic/molecular testing segment is growing **20% to 25%** per year as new applications are developed and commercialized. The market for cancer testing is also growing rapidly due to the following key factors:

- Cancer is the leading cause of death in the US and one in four deaths in the US is due to cancer. A total of 1,660,290 new cancer cases and 580,350 cancer deaths are projected to occur in the US in 2013 according to American Cancer Society;
- Cancer is primarily a disease of the elderly and now that the baby boomer generation has started to turn sixty, the U.S. is experiencing a significant increase in the number of senior citizens; The American Cancer Society estimates that one in four senior citizens will develop some form of cancer during the rest of their lifetime;
- Every year more and more genes are implicated in development and/or clinical course of cancer. These associations fuel the development of new genetic or molecular tests.

The total cancer testing market is approximately $10 billion to $12 billion in the US, and is growing very rapidly. Rosetta's primary focus is to provide **high complexity** and **high revenue** cancer molecular laboratory testing for patients.

In the US, the market of genetic/molecular testing is dominated by a few large companies that have recently consolidated numerous smaller players in the industry. There are approximately 300 genetic laboratories in the U.S., but most of them (approximately 80%) are affiliated with academic institutions and are focused on research and institutional needs. There are about 60 commercial labs in the US, and 40 - 50 are small privately-run labs and only 10 -20 are large, national or regional labs. The two largest of

these, **Quest Diagnostics** and **LabCorp** together make up approximately 40% of the cancer genetics testing market.

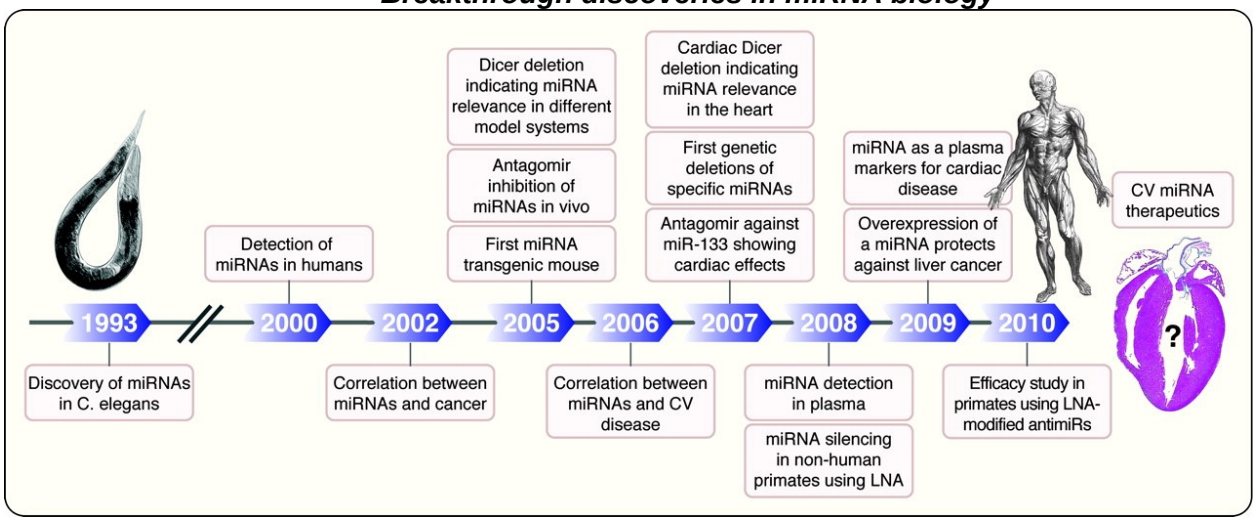
The microRNA Technology

Originally identified as moderate biological modifiers, microRNAs have recently emerged as powerful regulators of diverse cellular processes with especially important roles in disease and tissue remodeling.

Before the 1990s, miRNAs were an unappreciated class of small RNAs that were only thought to have a relevant function in non-mammalian species. The first published description of an miRNA appeared in 1993 by Lee RC, et al (Cell 75: 843-854). Since then, the breadth and diversity of this class of small, regulatory RNAs have been appreciated.

A great deal of effort has gone into understanding how, when, and where microRNAs are produced and function in cells, tissues, and organisms. Each microRNA is thought to regulate multiple genes, and since hundreds of miRNA genes are predicted to be present in higher eukaryotes, the potential regulatory circuitry afforded by microRNA is enormous. MicroRNAs may act as key regulators of processes as diverse as early development, cell proliferation and cell death, apoptosis and fat metabolism, and cell differentiation. There is speculation that in higher eukaryotes, the role of microRNAs in regulating gene expression could be as important as that of transcription factors.

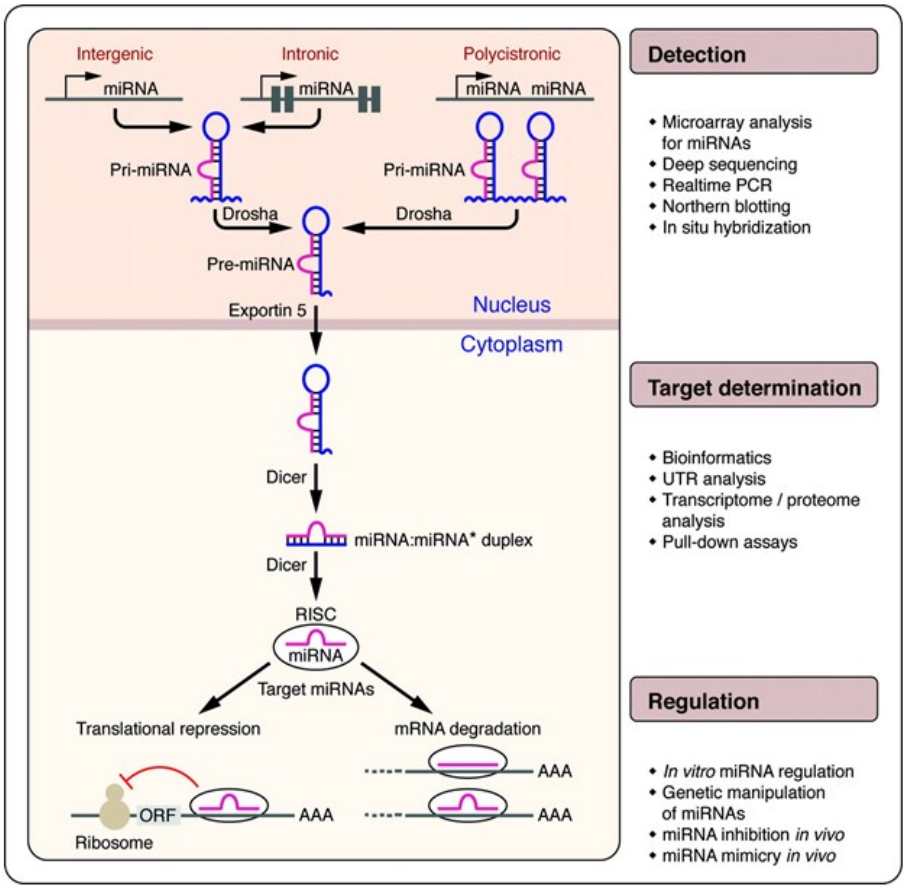
Breakthrough discoveries in miRNA biology



Source: van Rooij E Circulation Research. 2011;108:219-234

microRNAs (miRNAs) are small, RNA molecules encoded in the genomes of plants and animals. These highly conserved, ~21-NT RNAs regulate the expression of genes by binding to the 3'-untranslated regions (3'-UTR) of specific mRNAs. microRNAs are produced from either their own genes or from introns.

MiRNA biogenesis and research tools



van Rooij E *Circulation Research*. 2011;108:219-234

microRNAs have been found to regulate the expression of other genes by **binding to mRNA**. microRNAs have been shown to have varying expression levels across various pathological conditions, and offer a new class of highly sensitive and tissue specific biomarkers.

We believe that using microRNAs as diagnostic biomarkers will enable the development of diagnostic products that can provide more accurate and comprehensive information to doctors and patients. Currently, many diagnostic tests are designed to detect abnormal levels of **messenger RNAs** or **proteins**. We believe **microRNA-based tests** have the potential to be superior to these tests because it is believed that microRNAs are closer to the biological origin of disease and many studies have shown their involvement in disease processes, including the demonstration that microRNAs are both diagnostic and prognostic markers. A change in the expression level of a single microRNA may affect the activity of dozens of messenger RNA genes, which in turn may affect the level of hundreds of proteins. In addition, microRNAs are very tissue specific and very stable in body fluids and tissue samples.

Furthermore, extracting microRNAs from tissue and body fluid samples is more reliable than extracting messenger RNAs because of the greater stability of microRNAs. In addition, amplification technologies, such as PCR, can potentially increase the sensitivity of a microRNA-based diagnostic test by generating millions of copies of a particular microRNA and thereby making it easier for the test to detect the presence of the microRNA. Since amplification technologies cannot be used with proteins, therefore, microRNA-based diagnostic tests have the potential to be more sensitive than protein-based diagnostic tests.

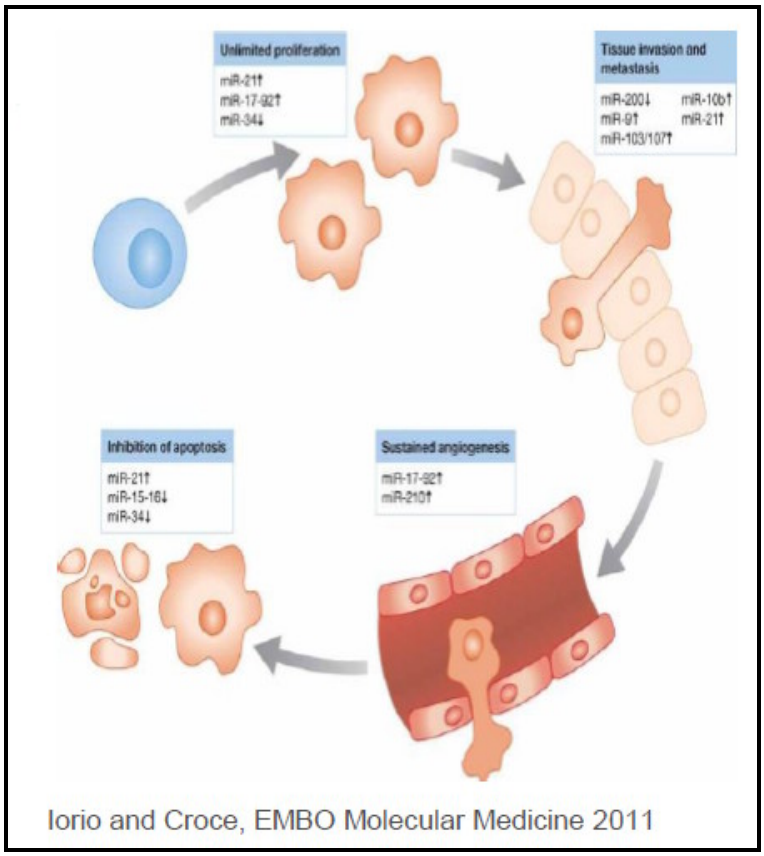
microRNAs also represent potential targets for the development of novel therapeutics.

MiRNAs Play a Central Role in Cancer

Thousands of peer reviewed papers reference the central role of microRNAs in cancer. microRNAs have been shown to be aberrantly expressed in all cancers.

microRNAs regulate the expression of their target mRNA, so that over- or under-expression of microRNAs is expected to respectively result in down- or up-regulation of the protein product of target mRNAs. It is easy to implicate a microRNA in a cancer if a direct target of a microRNA is an oncogene or a tumor suppressor.

Comprehensive microRNA profiles have been reported with clinical specimens from various cancers. Consistent with the notion that microRNAs are expressed in a tissue specific manner, microRNAs are different among cancers from various tissue origins. There are also a couple of microRNAs that appear to be frequently deregulated in many cancers, suggesting that these microRNAs regulate fundamental processes such as cell proliferation or apoptosis.



Iorio and Croce, EMBO Molecular Medicine 2011

Rosetta Genomics Is the Leader in MiRNA Platform

As a pioneer in the development of microRNA-based products, Rosetta has the most validated and accurate microRNA biomarker platform. Rosetta Genomics has developed **proprietary platform** technologies for the identification, extraction, quantification, and analysis of microRNAs from a wide range of sample types through innovation. This development effort has enabled the identification and advancement of multiple diagnostic projects addressing critical unmet needs in cancer, cardiovascular diseases and other indications. Rosetta Genomics is a leader in the intellectual property portfolio covering a large portion of known human and viral microRNAs.

Rosetta Genomics has put in place a unique development engine capable of rapidly advancing multiple diagnostic projects addressing critical unmet needs in **cancer** and other disease areas. The engine's main components are:

- Strong IP position provides access to hundreds of potential microRNA biomarkers.
- Proprietary discovery, extraction, and quantification technologies enabling the company to rapidly expand its pipeline.
- Extensive collaborations with leading research and knowledge centers providing the company with input from the forefront of clinical research as well as access to hundreds of sample types.

Rosetta Genomics has filed numerous patent applications protecting **composition-of-matter** for human and viral microRNAs, as well as **applications** protecting its **microRNA extraction protocols and diagnostic methods** using microRNAs. These patent applications are related to hundreds of human and viral microRNA sequences. The patent applications are directed to a wide range of variations, including mutations on the mature microRNA, the microRNAs' precursor and its predicted binding sites. In addition, the company's patent applications are also related to the predicted biological function of the microRNAs, and their uses in research, diagnostics and therapeutics. Rosetta has also **in-licensed** important composition-of-matter patents from the Max Planck Institute and Rockefeller University.

This broad IP position allows Rosetta Genomics to pursue multiple internal product development opportunities. In addition, the company's IP position can serve as a firm basis for its collaborators regarding a diverse range of collaborations and licensing opportunities in key areas not targeted by Rosetta for internal development.

The identification of microRNA biomarkers requires sensitive and specific measurements of the levels of the microRNAs extracted from the tissue or body fluid samples. Rosetta Genomics has developed proprietary methods to rapidly, robustly and accurately perform these measurements.

Once extracted, Rosetta's technology is capable of detecting and quantifying the microRNAs using two custom designed platform technologies which utilize **quantitative Real Time PCR** (qRT-PCR) and **microarrays**.

Rosetta's proprietary discovery **microarray platform** covers approximately 2000 human microRNAs, including approximately 170 microRNAs that are Rosetta Genomics' proprietary microRNAs. In addition to its high sensitivity, the array's high specificity allows discriminating homologous family members.

Rosetta's **qRT-PCR platform** offers unparalleled sensitivity and specificity, with the ability to detect microRNAs on the single molecule scale, and to discriminate homologous microRNA.

These proprietary technologies enable Rosetta Genomics to accurately measure specific microRNAs, and are the basis of its diagnostic development engines. By focusing its efforts on microRNAs, Rosetta Genomics can develop a less complex biomarker panel, resulting in a more specific and sensitive test.

Rosetta Cancer Origin Test™ (miRview® mets2)

Over the years, Rosetta has developed and launched six cancer diagnostics based on its proprietary microRNA technologies with four currently marketed versions of these tests. The Cancer Origin Test is the company's **lead cancer test**.



The Cancer Origin Test is the company's second-generation microRNA-based diagnostic for the identification of the primary site of metastatic cancer, specifically metastatic cancer of unknown or uncertain primary **(CUP).**

CUP is a heterogeneous group of cancers that constitutes 3-5% of all cancers with a poor median survival of six to ten months. Each year approximately 70,000 patients in the United States are diagnosed with CUP. A patient is typically diagnosed with CUP only after undergoing a wide range of tests, including various imaging tests such as x-ray, CT, MRI, and PET, which have failed to identify the origin of the cancer. Presently, the choice of treatment for metastatic cancer is largely dependent on the nature of the primary tumor. Patients with CUP pose a therapeutic dilemma and treatment is often empiric with a "one treatment fits all" approach. In the era of rapidly growing effective cytotoxic and targeted therapies for known cancers, quicker and more accurate methods to identify the tissue of origin of CUP cancers would permit the use of these therapies, thereby improving the chances of achieving a response and possibly extending the patient's survival.

Rosetta Cancer Origin Test utilizes custom-designed **microarray technology** to identify **49 possible cancer origins** with very high accuracy using **64 microRNAs**. These 49 origins include carcinomas, soft tissue tumors, lymphoma and other malignancies. This test is designed to help provide a diagnosis for cancer patients with unknown or uncertain primary origins.

The Cancer Origin Test is a product of more than five years of research analyzing hundreds of tumor samples. The test has been developed using rigorous methodology and validated using an independent blinded set of samples. The test is available in the United States, Canada and world-wide.

Rosetta Genomics has developed an innovative method to rapidly, robustly, and accurately extract microRNAs from a wide range of sample types. Currently, the Cancer Origin Test can be performed on formalin-fixed paraffin-embedded (FFPE) samples. The ability to extract microRNA from FFPE samples is key to the clinical applicability of Rosetta's cancer diagnostics. Because FFPE samples do not require special storage, they may be held at room temperature and sent for evaluation via standard shipping methods.

The Cancer Origin Test performance was determined in an independent, blinded test set of 509 samples. In the vast-majority of cases, the Cancer Origin Test returned a single tissue prediction with 90% sensitivity, 99% specificity and overall sensitivity was 85%. The high level of accuracy of the Cancer Origin Test is better than published data from competitors.

While many of the cancer tests currently available are largely qualitative and subjective, the measurement of microRNA expression levels in tissue samples offers a quantitative, objective diagnosis. Proprietary technologies enable microRNA profiling with high sensitivity and specificity, leading to **high level of accuracy**. In addition, microRNAs are stable markers in many body fluids and tissue samples, leading to lower failure rate, making them an ideal platform for molecular diagnostics.

Market potential is huge for the Cancer Origin Test. There are about 200,000 CUP and other metastatic disease patients who may benefit per year in the US. Rosetta Cancer Origin Test is covered by Medicare at a rate of about **$3,500/test.** Over 170 million lives are covered by both Medicare and commercial payors.

Rosetta Lung Cancer Test™

The Lung Cancer Test is a cutting-edge molecular diagnostic test that uses **8 microRNAs** to accurately differentiate **four subtypes of lung cancer.** It classifies neuroendocrine and non-small cell lung cancer (NSCLC); and then further subclassifies NSCLC to either squamous or non-squamous; and further subclassifies neuroendocrine to either small or carcinoid.



For patients with lung carcinoma, the accurate determination of tumor type significantly influences **treatment decision**. In general, SCLC, the main sub-type of neuroendocrine tumors, is much more responsive to chemotherapy and consequently this comprises the mainstay of treatment. This is in contrast to NSCLC which is relatively chemoresistant and thus primarily treated with surgical resection for local disease. In addition, the recent emergence of novel biological therapies that effectively target specific cellular alterations now demands the most precise classification possible for non-small cell carcinomas. For example, lung adenocarcinomas are more likely to respond to EGFR tyrosine kinase inhibitors (e.g. erlotinib). Similarly, antibody therapy (bevacizumab) directed against vascular endothelial growth factor (VEGF) is more effective in the treatment of adenocarcinomas. Not only is bevacizumab less effective in treating squamous cell lung cancers, but the squamous phenotype is associated with much higher rates of life-threatening pulmonary hemorrhage. Thus, the distinction of squamous from non-squamous carcinomas is becoming increasingly important.

However, current techniques and methods for lung cancer typing lack standardization, are difficult to reproduce and have an unacceptable level of variability between pathologists and laboratories. In particular, owing to limited tumor sample amounts and the poor quality of some samples, the classification of primary lung cancers using small preoperative biopsy specimens presents a diagnostic challenge using current tools.

THe Lung Cancer Test is a **microRNA-based** lung cancer classification test for cytology samples, mainly fine-needle aspirate (FNA) samples as well as pathology samples, such as small biopsies and resections. The test targets all newly diagnosed lung cancer patients.

Unlike current methods, The Lung Cancer Test is based on the expression levels of **eight microRNAs**, measured using a sensitive quantitative RT-PCR platform, and provides a differential diagnosis with fast, standardized and objective classification. A high level of accuracy was demonstrated in a validation study performed on 451 independent samples. This study determined the test's sensitivity and specificity to be 94% and 98%, respectively for the identification of the four main subtypes of lung tumors. The sensitivity for very small samples sizes (i.e., cytological samples) is 95% with a specificity of 98%.

Thus, the Lung Cancer Test is a simple and reliable diagnostic assay that offers an accurate and standardized classification tool for primary lung cancer using pathologic and cytologic samples, which helps doctors make informed patient care decisions.

Lung cancer is the second most common cancer in both men and women (not counting skin cancer) and is the leading cause of cancer-related death worldwide and in the United States. Lung cancer accounts for about 13% of all new cancers. The American Cancer Society estimates that there will be about 224,210 new cases of lung cancer, and 159,260 deaths from lung cancer in the US in 2014.

Rosetta Kidney Cancer Test™

The Rosetta Kidney Cancer Test™ is a cutting-edge molecular diagnostic test that utilizes microRNA expression to accurately differentiate **four main types of primary kidney tumors:** clear cell, papillary, chromophobe, and benign oncocytoma. In May 2012, Rosetta Genomics launched this microRNA-based kidney tumor classification test for pathology samples.



Subtypes of kidney tumors have different genetic backgrounds, prognosis and responses to surgical and medical treatment. Differential diagnosis between different types of kidney tumors can be challenging and can lead to unnecessary surgeries. There is a growing unmet medical need for kidney tumor classification. However, sometimes, it's difficult for pathologists to distinguish between tumor types on the basis of morphology and immunohistochemistry (IHC).

The Kidney Cancer Test uses the expression of **24 microRNAs** to accurately identify the kidney tumor subtype. The test was developed using 181 samples with blinded validation performed on 201 samples yielding a test sensitivity of 95%.

Kidney cancers account for more than 3% of adult malignancies. Each year in the US, there are about 65,000 new cases of primary kidney tumors and about 13,000 die from kidney cancer. The Kidney Cancer Test provides a differential diagnosis with fast, standardized and subjective classification and therefore helps doctors make more informed patient care decisions.

Rosetta Mesothelioma Test™

The Mesothelioma Test is a state-of-the-art molecular diagnostic test that uses **microRNA** to differentiate malignant pleural mesothelioma **(MPM,** often due to asbestos exposure**)** from **carcinomas** in the lung or pleura.



The mesothelioma test is a **medically** and **legally** important differential diagnosis.

The definitive identification of MPM from carcinomas has significant clinical implications. MPM is a solid, locally aggressive tumor of the lung pleura that covers and later invades the lung parenchyma, which leads to a severe clinically symptomatic disease. The incidence of mesothelioma has clearly grown in recent years in all developed countries of Western Europe, North America, and most probably in developing countries as well. Exposure to **asbestos** is still a major factor that contributes to the continuing growth in number of cases. As mesothelioma patients require specific treatment regimens, an accurate diagnosis is critical. However, the distinction between mesothelioma and carcinomas that involve the pleura, in particular peripheral pulmonary adenocarcinoma, can be challenging.

Over the past twenty years, immunohistochemistry has become the mainstay of the pathologic diagnosis of mesothelioma. However, because of the inter-observer variations between pathologists, and because of the absence of a single specific and reliable biomarker for the diagnosis of mesothelioma, the distinction between mesothelioma and carcinomas using **immunohistochemistry** can be difficult in

some cases. There is a need for a reliable and objective assay that would help make this distinction with greater confidence.

The Mesothelioma Test solves this problem by analyzing differential expression of microRNAs in mesothelioma and various carcinomas which generated high sensitivity and specificity. The test is conducted in a total of 243 samples (33 malignant pleural mesotheliomas, 210 carcinomas). Using **microarrays**, Rosetta identified microRNAs differentially expressed between **MPM** and various **carcinomas**. The assay reached a **sensitivity of 100%,** a **specificity of 94%** and a **100% negative predictive value** in a blinded validation set of 68 samples from the lung and pleura.

This assay provides a standardized, quantitative alternative to the currently applied methods. The small number of microRNAs needed for classification, the high tissue specificity of these microRNAs and the ease of their determination from archival fixed tissues embedded in paraffin, makes this assay a practical option. The microRNA-based assay that Rosetta has developed, uses expression levels of only **three microRNAs,** and is able to accurately diagnose mesothelioma and distinguish it from lung adenocarcinoma and other malignancies involving the lung and pleura with very high sensitivity and specificity. This assay is simple to perform and highly reliable in its reproducibility.

In addition to clinical applications, Rosetta Mesothelioma Test has a unique opportunity in mesothelioma **lawsuits**, which allows the company to charge high price for the test due to private pay from plaintiffs and defendants.

Each year in the US, there are about 2000 new claims arising from mesothelioma cases, and over 8000 pending claims.

An Appropriate Strategy Is In Place

Rosetta's goal is to become a leader in the development and commercialization of microRNA-based diagnostic tests. Its key business strategies to achieve this goal are as follows:

- Rosetta plans to **leverage** its extensive microRNA knowledge and experience to potentially develop additional tissue based as well as body fluid-based diagnostic tests.

- Maximize sales of current four commercial cancer tests through geographic **partners**. Rosetta plans to maximize revenues from its four current commercial tests via corporate relationships and through its own targeted commercial efforts. To date the company has entered into distribution agreements with five distributors, pursuant to which these distributors have the right to commercialize these tests in their territories. Rosetta intends to support the work of these partners while pursuing other partnerships for additional geographies.

- Build and maintain a strong **intellectual property** position. Rosetta is the first commercial enterprise to focus on the emerging field of microRNAs diagnostics. The company has an early and strong intellectual property position in the area of developing and commercializing microRNA-based diagnostic tests. Rosetta plans to seek broad coverage on all of its identified microRNA sequences. The company also has filed, and intends to continue to file, patent applications that claim its technical platforms and method-of-use for specific diagnostic and therapeutic applications.

- Rosetta intends to continue to establish **strategic collaborations** with leading clinical diagnostic and pharmaceutical companies to further develop and commercialize microRNA-based diagnostics. The company's strong intellectual property position and expertise in the field of microRNAs will be very attractive to additional collaboration partners.

In general, Rosetta is generating demand for its four cancer testing services, primarily its lead Rosetta Cancer Origin Test, through its direct selling effort in the United States. The company is successfully

fulfilling that demand in its lab in Philadelphia, Pennsylvania. The company's cancer origin test is already covered by Medicare and some commercial payors. Rosetta is working with its reimbursement vendor and consultants to gain more consistent payment from commercial payors, as well as to secure reimbursement coverage from Medicare for additional cancer tests.

Currently, Rosetta has established various distribution agreements with different companies to market its cancer tests outside the US.

All of these distribution and other agreements call for samples to be sent to Rosetta's CLIA-certified laboratory in Philadelphia, Pennsylvania for analysis.

PROJECTED INCOME STATEMENT

	2011A (Dec)	2012A (Dec)	2013A (Dec)			2014E (Dec)			2015E (Dec)	2016E (Dec)	2017E (Dec)	2018E (Dec)	2019E (Dec)	2020E (Dec)
$ in million except per share data	FYA	FYA	1H13	2H13	FYE	1H14	2H14	FYE	FYE	FYE	FYE	FYE	FYE	FYE
Total Revenues	**$0.10**	**$0.20**	**$0.19**	**$0.21**	**$0.41**	**$0.50**	**$1.00**	**$1.50**	**$5.50**	**$12.50**	**$25.00**	**$50.00**	**$80.00**	**$125.00**
YOY Growth	-63.1%	95.1%	278.4%	41.3%	101.5%	159.1%	371.7%	270.4%	266.7%	127.3%	100.0%	100.0%	60.0%	56.3%
CoGS	0.32	0.26	0.43	0.28	0.71	0.70	0.15	0.85	0.72	1.56	3.13	6.25	10.00	15.63
Gross Income	**($0.22)**	**($0.06)**	**($0.24)**	**($0.06)**	**($0.30)**	**($0.20)**	**$0.85**	**$0.65**	**$4.79**	**$10.94**	**$21.88**	**$43.75**	**$70.00**	**$109.38**
Gross Margin	-214.6%	-28.4%	-124.9%	-29.7%	-75.1%	-40.0%	85.0%	43.3%	87.0%	87.5%	87.5%	87.5%	87.5%	87.5%
R&D	$3.39	$1.25	$0.88	$0.87	$1.74	$1.10	$1.15	$2.25	$3.50	$5.00	$7.50	$10.00	$13.00	$15.50
% R&SD	3287.4%	620.4%	454.4%	409.0%	430.6%	220.0%	115.0%	150.0%	63.6%	40.0%	30.0%	20.0%	16.3%	12.4%
SG&A	$5.17	$6.96	$5.55	$5.75	$11.30	$6.50	$7.50	$14.00	$17.50	$20.00	$22.50	$25.00	$30.00	$45.00
% SG&A	-	3464.2%	2876.7%	2710.8%	2789.9%	1300.0%	750.0%	933.3%	318.2%	160.0%	90.0%	50.0%	37.5%	36.0%
Other Expense	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Operating Income	**($8.8)**	**($8.3)**	**($6.7)**	**($6.7)**	**($13.3)**	**($7.8)**	**($7.8)**	**($15.6)**	**($16.2)**	**($14.1)**	**($8.1)**	**$8.8**	**$27.0**	**$48.9**
Operating Margin	-8521.4%	-4112.9%	-3456.0%	-3149.5%	-3295.6%	-1560.0%	-780.0%	-1040.0%	-294.8%	-112.5%	-32.5%	17.5%	33.8%	39.1%
Other Net	($0.1)	($2.2)	$0.4	($0.2)	$0.2	$0.0	$0.0	$0.0	($0.5)	($0.5)	($0.5)	($0.5)	($0.5)	($0.5)
Pre-Tax Income	**($8.8)**	**($10.5)**	**($6.3)**	**($6.9)**	**($13.2)**	**($7.8)**	**($7.8)**	**($15.6)**	**($16.7)**	**($14.6)**	**($8.6)**	**$8.3**	**$26.5**	**$48.4**
Income taxes(benefit)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1.0	$4.5	$9.0
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	12.1%	17.0%	18.6%
Reported Net Income	**($8.8)**	**($10.5)**	**($6.3)**	**($6.9)**	**($13.2)**	**($7.8)**	**($7.8)**	**($15.6)**	**($16.7)**	**($14.6)**	**($8.6)**	**$7.3**	**$22.0**	**$39.4**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-184.1%	203.4%	79.0%
Net Margin	-	-	-	-	-	-	-	-	-	-	-34.5%	14.5%	27.5%	31.5%
Diluted Shares Out	0.5	4.4	9.2	10.0	9.6	9.8	10.0	9.9	15.0	17.5	20.0	22.5	25.0	30.0
Reported EPS	**($17.39)**	**($2.35)**	**($0.68)**	**($0.69)**	**($1.37)**	**($0.80)**	**($0.78)**	**($1.58)**	**($1.11)**	**($0.83)**	**($0.43)**	**$0.32**	**$0.88**	**$1.31**
One time charge	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*
Non GAAP Net Income	**($8.8)**	**($10.5)**	**($6.3)**	**($6.9)**	**($13.2)**	**($7.8)**	**($7.8)**	**($15.6)**	**($16.7)**	**($14.6)**	**($8.6)**	**$7.3**	**$22.0**	**$39.4**
Non GAAP EPS	**($17.39)**	**($2.35)**	**($0.68)**	**($0.69)**	**($1.37)**	**($0.80)**	**($0.78)**	**($1.58)**	**($1.11)**	**($0.83)**	**($0.43)**	**$0.32**	**$0.88**	**$1.31**

Source: Company filing and Zacks estimates

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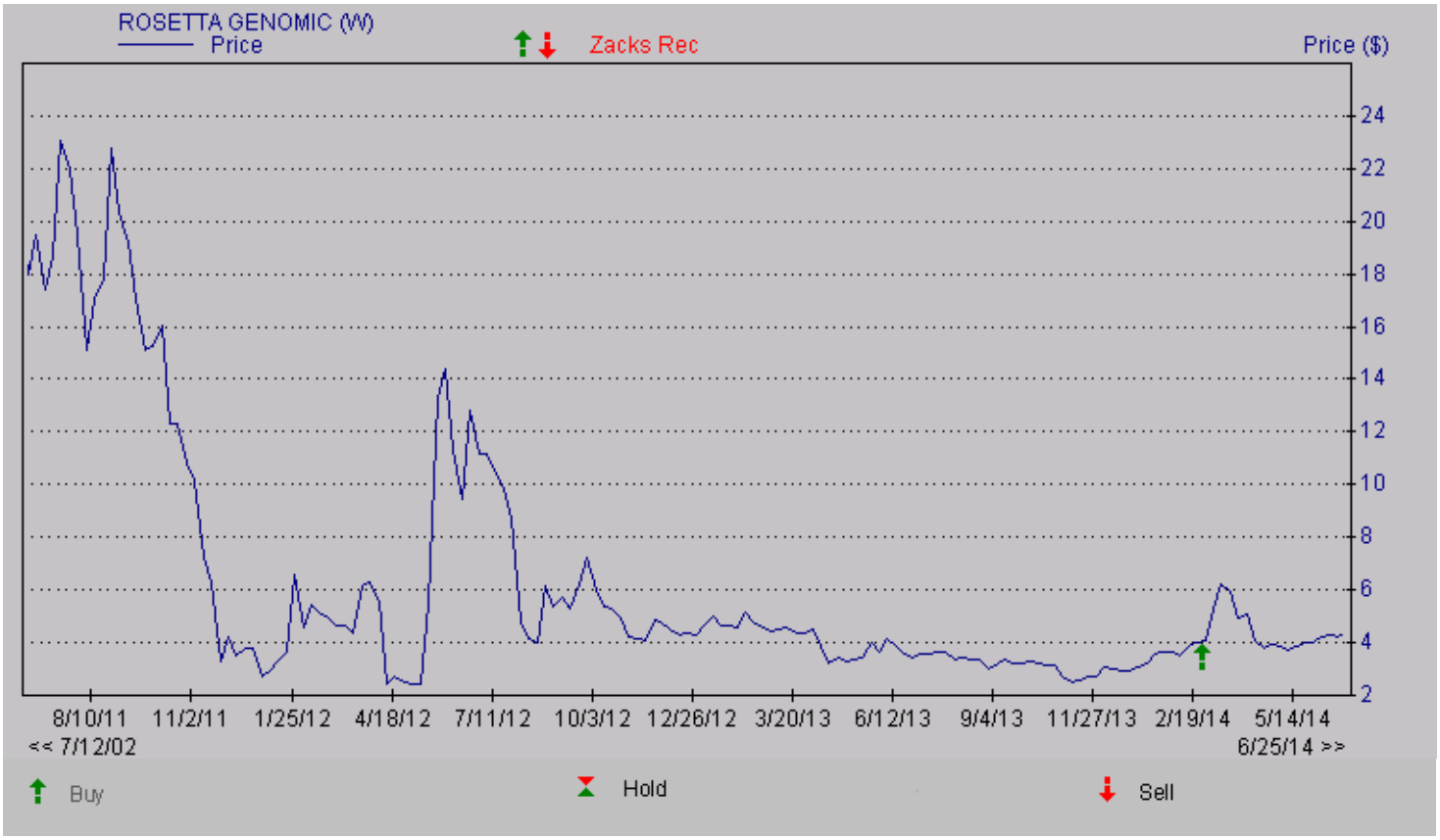

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