Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Roche to Acquire Ventana for $3.4 Billion

Nearly a year after beginning talks with Tucson, Arizona-based Ventana Medical Systems, Roche (Basel, Switzerland) announced on January 22 that it has entered into a merger agreement to acquire the tissue-based diagnostics company for $89.50 per share in cash (approximately $3.4 billion on a fully diluted basis). The per-share deal price, up from Roche's initial $75 per share offer, represents a 4.9% premium to Ventana's closing price on January 18 and a 72.3% premium to the closing price on June 22 of last year, the last trading day before Roche made its initial offer. The merger agreement has been approved by the boards of Ventana and Roche.

The acquisition of Ventana, which has yet to report its revenue for 2007 (estimated at $297 million), will broaden Roche's diagnostics offerings and complement its oncology therapies. After the completion of the transaction, Christopher Gleeson, Ventana's president and chief executive officer, will continue as CEO of Ventana's business and become a member of the Roche Diagnostics executive committee. Ventana will remain in Tucson, and its employees will become part of the combined company. For more on Roche and its recently announced 2007 results, see *Inside the Diagnostics Industry*, pp. 4-6.

Autogenomics Gets FDA Clearance for Infiniti Assays

Privately held Autogenomics (Carlsbad, CA) has received 510(k) clearance from the U.S. Food and Drug Administration (FDA) to market two DNA tests that are run on the Infiniti system, the company's microarray-based multiplexing molecular diagnostic platform.

The two FDA-cleared assays qualitatively detect: 1) genetic mutations in Factor II (Prothrombin) and Factor V Leiden, and 2) genetic mutations in cytochrome P450 2C9 (CYP2C9) and vitamin K epoxide reductase complex subunit 1 (VKORC1) that confer sensitivity to warfarin. According to the FDA, the former assay is indicated for use as an aid to diagnosis in the evaluation of patients with suspected thrombophilia, while the latter is indicated for use to identify individuals at risk for sensitivity to warfarin, the popular oral anticoagulant.

Last August, Autogenomics received FDA clearance to market its Infiniti analyzer, an automated, multiplexing, continuous flow, random access microarray platform that integrates such processes as sample handling, reagent management, hybridization, and detection into a self-contained system. The analyzer works by measuring fluorescent signals of labeled DNA target *Continued on p. 2*

▲ **FDA Clearance for Infiniti Assays,** *from page 1*

hybridized to novel, film-based microarrays known as BioFilmChips. It is equipped with a built-in confocal microscope, a thermal stringency station, and a temperature cycler.

Autogenomics plans to file for FDA clearance for additional applications in its expanding Infiniti test menu in pharmacogenetics, genetic disorders, infectious diseases, and cancer diagnostics. Assays now in clinical validation include those for human papilloma virus, cystic fibrosis, and genetic variants in the multi-drug resistance gene (MDR-1), uridine diphosphate glucuronosyltransferaseisoform 1A1 (UGT1A1), and various cytochrome P450 subtypes.

New Biomarker Linked to Warfarin Dose Requirements

In three independent studies, a novel DNA variant in cytochrome P450 4F2 (CYP4F2) was found to alter the required dose of warfarin, the commonly prescribed anticoagulant that is used to treat and prevent thrombotic events. The research was prepublished online in *Blood* on February 4. The molecular diagnostics company Osmetech (Pasadena, CA, and London) licensed the CYP4F2 biomarker from the Marshfield Clinic Research Foundation (Marshfield, WI) last November and anticipates adding it to its warfarin genotyping test, which is awaiting pre-marketing regulatory clearance by the United States Food and Drug Administration (FDA).

Warfarin has been used widely for over 50 years, but it is remains one of the trickiest drugs for physicians to prescribe because of the inter-individual variability in degree of anticoagulation achieved in response to the same dose. Warfarin dosing variability has been linked to variants in CYP2C9 and the vitamin K 2,3 epoxide reductase complex 1 (VKORC1). Last year, the FDA mandated the relabeling of warfarin to note the usefulness of genetic testing for these two genetic markers to optimize dosing and lower the risk of adverse events. Existing pharmacogenetic models explain just over half of the variation in warfarin dosing.

Every year, about 2 million patients in the United States begin warfarin therapy, according to estimates by the U.S. Food and Drug Administration.

Using microarrays, researchers at three sites screened a total of 1,054 patients that had been stabilized on warfarin to explore whether additional single-nucleotide polymorphisms (SNPs) were affecting warfarin dose requirements. After adjusting the SNPs for known clinical factors and CYP2C9 and VKORC1, they identified CYP4F2 as having a statistically significant association with warfarin therapeutic dose. Patients with this gene variant were found to require about 1 mg/day more warfarin than patients without it. CYP4F2's function in warfarin metabolism is unknown.

In the paper, the authors note that, "Because of differences in the frequency of the underlying genetic variants among major racial groups, the potential benefit from prospective CYP4F2 genotyping varies by race." The CYP4F2 variant appears more frequently in Caucasians and Asians than in African-Americans.

The researchers do not present a clinical model that uses CYP4F2 to prospectively

dose patients initiating warfarin therapy, but such models are expected to be developed as more data become available.

The research comes as particularly good news for Osmetech, which has an exclusive license for CYP4F2 and plans to develop, manufacture, and sell a genetic test based upon the findings. "This marker in conjunction with variants from [CYP2C9 and VKORC1] . . . will improve patient outcomes by reducing the overall complications of warfarin therapy, reducing costs in the health system, and helping provide a new standard of personalized care," says Osmetech CEO James White. "The fact that Osmetech has an exclusive license to this marker for warfarin testing, we believe will help position us as the leading diagnostic company in this area."

In January, Osmetech submitted its eSensor 2C9/VKOR test to the FDA for 510(k) pre-marketing clearance. The genotyping test, which is run on the company's eSensor X-T8 instrument, is for the CYP2C9 and VKORC1 gene variants, but the company plans to eventually add testing for the new CYP4F2 marker to its X-T8 platform.

LabCorp Acquires CRO, Focuses on Companion Diagnostics

The nation's second largest provider of diagnostic testing services, LabCorp (Burlington, NC), has entered into a definitive agreement to acquire Tandem Labs (Salt Lake City), a bioanalytical contract research organization (CRO) working with pharmaceutical and biotechnology companies on discovery, preclinical, and clinical drug development programs. Tandem Labs—which also has facilities in West Trenton, New Jersey, and Woburn, Massachusetts—will operate under LabCorp's Esoterix clinical trials group and will maintain its existing name, along with current employee and management structure. Financial terms of the transaction were not disclosed.

Both LabCorp and Quest Diagnostics appear to be focusing more on clinical trials work. Quest has indicated that its emerging operations in India will include clinical trials testing work for pharmaceutical companies. However, LabCorp spokesman Erik Lindblom called the Tandem acquisition more of a strategic move to focus on developing and bringing companion diagnostics to market, rather than expanding the clinical trials business, which he said has been growing in recent years.

And more acquisitions are likely ahead for LabCorp. At the JPMorgan Healthcare Conference in San Francisco in January, CEO David P. King noted, "Industry acquisition and consolidation continue to be both a driver of top-line revenue and growth for [LabCorp], as well as an appropriate use of cash."

King also said that the company is looking at expanding managed care contracts. "When we think about revenue drivers in the short- and mid-term . . . the major driver of revenue expansion for us is expanding our managed care contracts, not just our UnitedHealthcare partnership, but our ability to market [our services] in all major markets for Cigna in 2008 will be a significant opportunity for us to expand our managed care footprint." Beginning in 2008, LabCorp will be able to market its services to 95% of Cigna providers, compared to 40% last year.

Roche Diagnostics Posts 6% Revenue Growth in 2007, Rising CEO Discusses Strategy

Severin Schwan

Roche Group (Basel, Switzerland) reports that sales at its diagnostics division grew by 6% in local currencies (7% in Swiss francs, 12% in U.S. dollars; unless otherwise stated, growth rates are in local currencies) last year to 9.350 billion Swiss francs (USD $7.800 billion); operating profit was up 14% to 1.648 billion Swiss francs (USD $1.375 billion). Meanwhile, sales at Roche's pharmaceutical division grew by 11% (13% excluding Tamiflu pandemic sales to governments and corporations, which declined significantly in the second half of the year due to early stockpiling), and operating profit was up by 22% to 13.042 billion Swiss francs (USD $10.880 billion) in 2007. Fritz Humer, chairman and CEO of Roche, called the pharmaceuticals division "clearly the main growth driver," noting that it grew approximately twice as fast as the market.

Diagnostics Growth Driven by New Products and Strategic Deals

"For diagnostics, 2007 has really been an extraordinary year," said Severin Schwan, the head of Roche Diagnostics who will take over as CEO of the entire group at the company's general meeting on March 4, on a conference call with analysts and reporters on January 30. He noted that the division's growth is driven by both new products and strategic transactions and described the in vitro diagnostics market as having changed significantly over the past two years. "We've seen an unprecedented number of M&A deals and new players such as Siemens now holding the number-two position."

Roche Diagnostics 2007 Financial Results

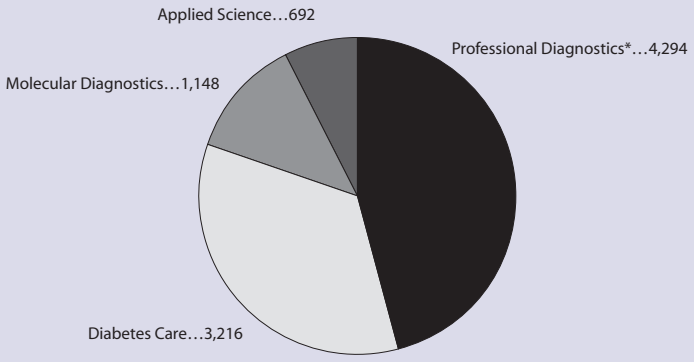
	In millions of CHF	In millions of U.S. dollars	YOY% Change in local currencies
Total diagnostics revenue	9,350	7,800	6
Professional Diagnostics*	4,294	3,582	8
Diabetes Care	3,216	2,683	5
Molecular Diagnostics	1,148	958	-2
Applied Science	692	577	11
Operating profit	1,648	1,375	14

*Amalgamation of Centralized Diagnostics and Near Patient Testing
Source: Roche

In 2007, Roche's professional diagnostics (centralized diagnostics and near patient testing combined) and diabetes-care businesses posted single-digit sales increases of 8% and 5%, respectively. Schwan noted that the performance of the professional diagnostics area was primarily due to growth in immunochemistry, driven by strong instrument placements and the market's embrace of new markers, such as N-terminal prohormone brain natriuretic peptide (NT-proBNP). "Diabetes care is positively turning around, after we had a decline in 2005," said Schwan, pointing to such new products as the Accu-Check Aviva blood glucose monitoring system.

As expected, pressure on industrial reagent prices continued to affect the sales of Roche's molecular diagnostics business, which was down 2% for the year. Excluding industrial reagents, which has sharply declined due to the expiry of patents on polymerase chain reaction (PCR), the area posted 3% top-line growth. Within the molecular diagnostics area, sales of virology products rose 4% in 2007, fueled by the continued success of the automated Cobas AmpliPrep/Cobas TaqMan (CAP/CTM) platform, which Roche launched in the United States and Japan last year. In the blood screening segment, full-year sales were down 1% in a competitive market that is feeling intense pricing pressure.

Roche Diagnostics 2007 Sales by Business Area
(in millions CHF)



*Amalgamation of Centralized Diagnostics and Near Patient Testing
Source: Roche

The applied sciences area grew at 11% in 2007, which Schwan attributed to growth in the DNA sequencing business. Last year saw the broad rollout of the company's Genome Sequencer FLX system.

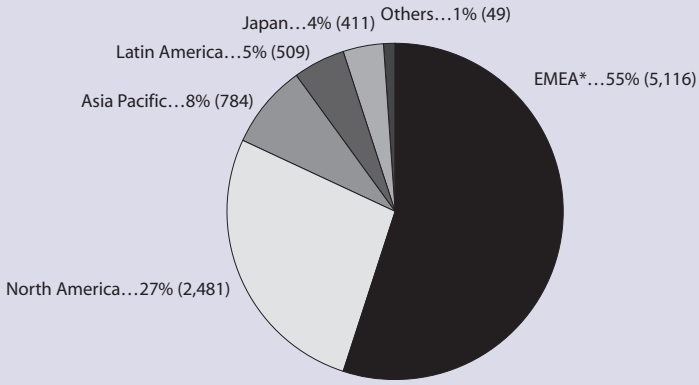
On a geographic basis, Roche Diagnostics saw its strongest growth in Latin America and Asia Pacific, where sales were up 19% and 18%, respectively. Both North America and EMEA (Europe, Middle East, and Africa) grew by 5%, while local sales in Japan were up by 2%.

On the mergers and acquisitions front, "We have completed our portfolio of key technologies," said Schwan, referring to the 2007 acquisitions of 454 Life Sciences, BioVeris, and NimbleGen Systems, as well as the company's pending merger with Ventana Medical Systems (*see p. 1*), which will mark Roche's entry into tissue-based diagnostics. "With those transactions, we could strengthen on the one hand the core business in our life sciences and in vitro diagnostics franchises, but I think that very important in this context is that now diagnostics can also better support pharma along the full-value chain, from discovery to commercialization of drugs," added Schwan.

Bridging Diagnostics and Pharmaceuticals

At a follow-up meeting with analysts and reporters in New York City on February 1, Schwan elaborated on aspects of Roche's 2007 results and discussed broader strategic issues, including the relatively new collaboration between diagnostics and pharmaceuticals. He emphasized the importance of beginning such collaboration early in the drug development process. "It's not like you to develop the drug, and then at the very end of the process, you do a companion diagnostic," said Schwan. "It's at the discovery phase where you start to develop certain hypotheses [about] biomarkers, where you need assays and different technologies to profile the drugs already in their early phase. And that's something that we looked into over the last two years in a very systematic way."

Roche Diagnostics 2007 Sales by Region
(in millions CHF)



*Europe, Middle East, and Africa
Source: Roche

He explained that for every pharma project at Roche, there is a dedicated milestone early in the process that involves looking for related biomarkers. "This does not necessarily mean that we'll end up with a biomarker," he cautioned. "And this certainly does not mean that eventually you will end up with a companion diagnostic test, but

Severin Schwan

it is now part of our normal process…to look at the potential in this field for every compound."

In discussing the Ventana deal, Schwan compared the long-term potential of the tissue-based diagnostics business to personalized medicine. "There's an element of integrating an attractive business as it is, but if you look at the [purchase price] you can hardly justify the premium just on the business," he said. "There must be on top of it a strong, basic belief in the long-term—otherwise you just can't make the numbers."

Pursuing a Targeted Approach

Schwan also answered questions about Roche's position on the strategies of other (unnamed) IVD companies. When asked about personal genomic profiling, now offered by such companies as deCODE Genetics and 23andMe, Schwan noted Roche's early, substantial investments in the area and its subsequent decision to refocus. "There are fundamental questions: What do you do if you have a predisposition but you don't have a drug? What is it worth? Who will pay for it?" asked Schwan. "This kind of broad-based, shotgun approach, where you kind of measure everything in the hope that something comes out, we're very skeptical on that side."

"Now diagnostics can better support pharma along the full value chain, from discovery to commercialization of drugs."

He was similarly dubious about the prospects for home testing and integrating healthcare management businesses with diagnostics, a strategy championed by Inverness Medical Innovations. He pointed to the higher cost of point-of-care and home-based testing, but noted that, "where it does play a role is those areas where speed is of the essence and where you do have an additional medical value if you have a fast result." To that end, Roche has focused its near patient testing in the areas of coagulation and glucose monitoring.

Consumer Marketing: Don't Bet on It

Finally, Schwan weighed in on the nascent trend of marketing diagnostic tests to patients. He noted that this trend is skipping from the traditional marketing target, the laboratory director, to the patient. "Before you would go to the patient, I think that there's a level in between and that is the physician," said Schwan. "And I do see an opportunity in getting a pull effect, if you like, by medical marketing via the physician." He provided the example of the cardiac market NT-proBNP as a test that was driven by the demand of the physicians and not the traditional customer in the lab.

As for whether the diagnostics sector would see a deluge of consumer marketing, Schwan believes that it will succeed in "very limited cases," pointing to Digene's marketing of its HPV test as one success story. "But I don't think this will turn into a big wave," he said. "At the end of the day, it's still a pretty complicated matter and very difficult to communicate to the patient, and the patient would normally for diagnostics rely more on the physician than the newspapers."

Recent Roche Diagnostics M&A

Transaction Date	Company	Expertise
May 2007	454 Life Sciences	Gene sequencing
June 2007	BioVeris	Electrochemiluminescence IP, expansion into clinical trials testing market
August 2007	NimbleGen Systems	High density microarrays
January 2008 (pending)	Ventana Medical Systems	Tissue-based diagnostics

Focus On: Cancer Diagnostics

In the second of this year's new bimonthly special topic supplements, DTTR *focuses on recent developments in cancer diagnostics, from the discovery of important information about the clinical significance of BRCA mutations and plans for a quantitative, mass spectrometry-based HER2 test to a promising new urine test for early cancer detection and commercial launches by deCODE Genetics, CombiMatrix, and Clarient. The breadth of these stories represents the many fronts on which cancer diagnostics is expanding, as new technologies and information about the disease process are translated to advancements in early detection, personalized treatment, and clinical decision making.*

deCODE Launches Genetic Test for Prostate Cancer

deCODE Genetics (Reykjavik, Iceland) has launched deCODE PrCa, a reference laboratory test for common, single-nucleotide polymorphisms (SNPs) that are associated with increased risk of prostate cancer. Performed exclusively by deCode's CLIA-certified reference lab, the test is priced at $500, which includes sample shipping costs. At this time, the test's results are applicable only to white European males since research data are not currently available for other ethnicities for all the variants.

> ***"This is a very big step because we have a test in humans to determine the risk of getting breast or prostate cancer long before the tumor appears."***

deCODE PrCa detects a total of six previously discovered SNPs, as well as two SNPs on chromosomes X and 2 that are reported by deCODE scientists in a paper published February 10 in the online edition of *Nature Genetics*. Most of the more common variants individually confer moderate risk of developing prostate cancer, but reach clinically significant risk levels when combined. Because of these variants, 10% of men are at twice the risk and 1% of men are at three times the risk of the disease in the general population.

"Through deCODE PrCa, we are bringing together in one tool all of the major genetic risk factors for prostate cancer that we have discovered over the past 18 months," says Kari Stefansson, CEO of deCODE. "We believe that this is a test with significant clinical utility for improving and personalizing the screening and treatment of one of the most common cancers." The company also plans to integrate the prostate cancer discovery into deCODEme, its consumer-directed personal genome analysis service.

deCODE PrCa is the latest in a series of reference laboratory DNA-based tests for assessing risk of and improving prevention and treatment for common diseases. The company's reference laboratory also performs DNA-based tests for type 2 diabetes, atrial fibrillation and stroke, and heart attack.

Estrogen-Based Test Could Detect Cancer at Earliest Stage

New research on the cellular triggers of cancer could help in the assessment, prevention, and detection of the disease. Using a urine-based test in humans, researchers have found that certain estrogen metabolites can react with DNA to cause damage that may lead to breast, prostate, and other cancers. The findings were published in the

December issue of the *International Journal of Cancer* and confirmed in a second, larger study presented at the recent San Antonio Breast Cancer Symposium.

Estrogens can initiate cancer when natural mechanisms of protection do not work properly in the body, allowing estrogen metabolites to react with DNA and induce cancer-causing mutations. "Now that we have the basic knowledge about this unifying mechanism of cancer initiation, we have a greater sense of urgency to assess people at risk and, at the same time, begin studies of prevention by using specific natural compounds," said Ercole Cavalieri, Ph.D., of the University of Nebraska Medical Center (UNMC; Omaha, NE).

The estrogen metabolites form estrogen-DNA adducts, which eventually make their way out of cells and are excreted in urine. The screening test developed by the researchers analyzes estrogen metabolite profiles in humans and can simultaneously associate the profile with risk of getting breast cancer. It involves testing a one-ounce sample of urine, using tandem mass spectrometry, which analyzes about 40 estrogen-related compounds, including estrogen-DNA adducts formed by a chemical reaction of estrogen metabolites and DNA.

The studies demonstrate how women at high risk of breast cancer can be identified by the level of adducts in a urine sample. Researchers analyzed estrogen-DNA from 46 women with normal risk for breast cancer, 12 women at high risk of developing breast cancer, and 17 women diagnosed with breast cancer. They found women at high risk of breast cancer and the women with breast cancer had significantly higher levels of the estrogen-DNA adducts in their urine samples, while the women with normal risk for breast cancer had low levels.

"This is a very big step because we have a test in humans to determine the risk of getting breast or prostate cancer long before the tumor appears," said Cavalieri. "We can use these estrogen-DNA adducts as a measure of cancer risk."

The discovery of a novel urine biomarker that appears to correlate with a women's risk of developing breast cancer has both diagnostic and therapeutic implications. Kenneth Cowan, M.D., Ph.D., director of the UNMC Eppley Cancer Center notes, "While these studies need to be confirmed in a prospective study in a larger group of patients, this could become an important screening assay for women and could lead to new therapies to prevent breast cancer."

Expression Pathology Developing Quantitative Test for HER2

Privately held Expression Pathology (Gaithersburg, MD) is developing a quantitative assay for human epidermal growth factor receptor 2 (HER2) in breast cancer. The tissue microproteomics company announced in early February that it had obtained $125,000 in funding from the state of Maryland to further the project.

Approximately 25% of breast cancer patients have HER2-positive tumors. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. Genentech's

According to the American Association for Cancer Research, approximately 40,000 women are diagnosed annually in the United States with HER2-positive breast cancer.

cancer drug Herceptin (trastuzumab) is targeted to HER2-positive tumors.

The new assay will use the company's proprietary sample preparation methods, reagents, and laser microdissection slides to extract proteins from standard formalin-fixed tissue. Rather than rely on visual interpretation of tissue staining patterns, the proteins will then be analyzed using mass spectrometry techniques.

"We believe that diagnostic assays utilizing mass spectrometry for tissue analysis have the potential to greatly improve patient treatment decisions, especially in cancer, where tissue biopsy and surgery are routine," said Casey Eitner, EPI's president and chief executive officer. "New quantitative tissue protein assays for analytes such as HER2 will be of tremendous interest for cancer research, but will also have a wide application in clinical trials and patient diagnostics."

CombiMatrix and Clarient to Offer DNA Test for Leukemia Prognosis

CombiMatrix (Mukilteo, WA) and Clarient (Aliso Viejo, CA) plan to jointly sell and market HemeScan, a genetic test to determine prognosis of patients with chronic lymphocytic leukemia (CLL), the most common form of adult leukemia. Using comparative genomic hybridization technology on a bacterial artificial chromosome (BAC) array, the test is designed to detect all of the known recurrent genomic abnormalities associated with CLL prognosis while providing a global view of the tumor genome.

Currently, there are approximately 60,000 people in the United States living with CLL, according to American Cancer Society estimates.

Characterized by the production of atypical lymphocytes, CLL is often difficult to manage because of its broad range of disease characteristics and outcomes. Using samples from bone marrow, HemeScan assays all of the genomic loci for copy number aberrations and incorporates recently identified genomic markers that may be useful in predicting the course of the disease. Researchers have validated HemeScan for use in patients with CLL, as well as acute lymphoblastic leukemia and myelodysplastic syndrome. Current testing is underway for use of HemeScan in multiple myeloma.

Based upon the patient's genetic test results, HemeScan categorizes that patient according to levels of prognostic risk, using an International Prognostic Scoring System (IPSS). The IPSS score stratifies the patient into "good," "intermediate," and "poor" risk categories to best inform the disease management process.

The test was developed by CombiMatrix in collaboration with several academic medical centers, including M.D. Anderson Cancer Center. Clarient plans to market the test to pathologists, oncologists, and patients.

"The HemeScan test's technology represents a more precise platform adding greater granularity to assist local pathologists and oncologists in the molecular assessment of this complex disease," said Ken Bloom, M.D., Clarient's chief medical officer. "The traditional cytogenetic test used currently does not reliably give us the information we need to take advantage of the therapeutic capabilities available today. Transitioning the industry to more sophisticated technologies undoubtedly will be a major step in providing personalized therapy for individual patients."

Usefulness of Cancer Preventing Surgery Differs Based on Gene Mutations

The efficacy of surgical removal of the ovaries to reduce the risk of breast and gynecologic cancers in women with BRCA1 and BRCA2 gene mutations differs based on mutation status, according to a study in the March 2008 issue of the *Journal of Clinical Oncology*. In addition to having important implications for women considering specific cancer-risk-reduction options, the findings add an important new layer of information to genetic test results.

The impact of surgical removal of the ovaries—or risk-reducing salpingo-oophorectomy (RRSO)—was analyzed in a multisite study led by researchers at Memorial Sloan-Kettering Cancer Center (MSKCC). Unlike previous studies, this one analyzed BRCA2 mutation carriers separately from BRCA1 mutation carriers. Researchers compared the incidence of breast and gynecologic cancers between a group of 509 women 30 years of age or older who carried a BRCA1 or BRCA2 mutation and had undergone RRSO and a group of 283 women with these mutations who did not have the surgery.

After following the women over three years, the researchers found that RRSO was associated with a 72% breast cancer risk reduction in women with BRCA2 mutations—nearly twice the reduction in breast cancer risk compared to women with BRCA1 mutations. The surgery also reduced the risk of gynecologic cancer by 85% in women with a BRCA1 mutation. Researchers were unable to estimate the level of reduced risk in women with a BRCA2 mutation due to the low incidence of gynecologic cancers among this group; however, protection against gynecologic cancer was suggested in the group.

Further analyses demonstrated that RRSO appeared to reduce the risk of estrogen receptor (ER)-positive breast cancer by 78% in women with a mutation in either BRCA1 or BRCA2, but had no effect on the development of ER-negative breast cancers. Because BRCA1 carriers are more likely to be diagnosed with ER-negative breast cancers, the authors note that carriers of these mutations need to consider additional breast-cancer-risk-reduction strategies, such as intensive screening with breast MRI.

"These findings will allow doctors to better tailor risk-reduction approaches for women at inherited risk for breast and ovarian cancer," said the study's lead author, Noah Kauff, M.D., a gynecologist and geneticist at MSKCC. "Given these results, further studies evaluating the efficacy of risk-reduction strategies in BRCA mutation carriers will likely need to stratify by the specific gene mutated."

Inverness to Acquire Matria Healthcare in $1.18 Billion Deal

"We are in the process of merging the notion of rapid diagnostic testing in the home with services being provided in the home to form sort of an unusual company…"

Inverness Medical Innovations (Waltham, MA) is continuing its roll-up strategy. The expanding global diagnostics company has signed an agreement to acquire Matria Healthcare (Marietta, GA), a national provider of health enhancement, disease management, and high-risk pregnancy management programs and services. Inverness will pay $39 per share of outstanding Matria common stock, a 27% premium over the previous day's closing price of $30.69. Inverness values the transaction at approximately $1.18 billion, which consists of approximately $900 million to acquire the stock as well as assumption of approximately $280 million of Matria's debt. Structured as a merger of an Inverness subsidiary with Matria, the deal is expected to close during the second quarter of 2008.

"We are in the process of merging the notion of rapid diagnostic testing in the home with services being provided in the home to form sort of an unusual company that looks after the patient in the home, while at the same time lowering costs to the payer," said Ron Zwanziger, CEO of Inverness, at the UBS 2008 Global Healthcare Services Conference on February 13 in New York City.

The proposed acquisition of Matria is another sign of six-year-old Inverness's faith in the home healthcare market for diagnostics. The company plans to consolidate Matria with its two other health management businesses—Alere and Paradigm—to focus on the growing health management market.

"Matria brings specialized expertise in women's health, which will complement our rapid diagnostics in that area," said Zwanziger. "Additionally, Matria's oncology services are the market leader in value-added services for oncology and fit with our Paradigm acquisition and with Paradigm's complex case management capability in oncology and neonatal intensive care. Coupled with Alere's market leadership position in cardiac disease, the addition of Matria provides Inverness with health and disease management market leading positions in women's health, oncology, and cardiology, three critical areas of strategic focus for Inverness."

Matria was founded in 1970 by Parker H. "Pete" Petit. Through its health enhancement and women's and children's health divisions, the company provides services to more than 1,000 employers and managed care organizations. In 2006, Matria reported revenues of $336.1 million. The company has yet to announce its full-year results for 2007.

Labs File Lawsuit to Stop Competitive Bidding Demo

Three San Diego clinical laboratories have filed a lawsuit in an attempt to stop the federal government from moving forward with its competitive bidding demonstration project for clinical laboratory services.

Filed by Internist Laboratory of Oceanside, Sharp Healthcare of San Diego, and Scripps Healthcare of San Diego against U.S. Department of Health and Human Services Secretary Michael Leavitt, the lawsuit also seeks to require public notice and comment on the project, as mandated by federal law.

The Centers for Medicare & Medicaid Services (CMS) chose the San Diego, Carlsbad, and San Marcos (California) communities as the test site for "competitive bidding" of clinical laboratory services. CMS will accept bids on laboratory services and select only a very limited number of labs to perform tests that will be reimbursed under Medicare Part B. Those labs not selected cannot be reimbursed for performing Medicare lab services.

"This lawsuit raises serious legal concerns and shows that something needs to be done to stop this reckless government experiment from moving forward," said Dr. Mark Birenbaum, administrator for the National Independent Laboratory Association and a member of the Clinical Laboratory Coalition (CLC).

Researchers Propose Gene-Based Approach to Diagnosing Autism

Autism and related disorders are usually diagnosed based upon behavioral factors, but a new stepwise approach promises a specific genetic diagnosis in approximately 40% of patients with autism-spectrum disorders, according to a report published in the January issue of *Genetics in Medicine*, the journal of the American College of Medical Genetics (ACMG). Clinical genetic evaluation using existing methods yields a 15% rate of diagnosis.

"For many practical reasons, a stepwise (tiered) evaluation is the preferred approach—rather than performing a 'shotgun' evaluation in which dozens of tests are ordered as a matter of routine," write the paper's authors, G. Bradley Schafer, M.D., of the University of Nebraska and Nancy J. Mendelsohn, M.D., of Children's Hospitals and Clinics of Minnesota. "In our experience, this approach has a high level of acceptance with third-party payers and with families."

The genetic evaluation approach has three steps and is intended to be used after pre-evaluation by a professional trained in autism diagnosis. The first tier of genetic evaluation includes tests that should be performed in nearly all children with no obvious cause of autism—for example, tests for fragile X syndrome, inherited metabolic disorders, and rubella infection. If these tests do not yield positive results, testing enters the second tier, which includes tests for specific gene mutations known to cause autism. If necessary, testing proceeds to the third tier, possibly including an MRI scan of the brain.

While payers may question the cost-effectiveness of genetic testing for autism, Schaefer and Mendelsohn believe their approach to genetic diagnosis will have significant benefits for families affected by the condition. The results could, for example, provide important information on the risk of autism in future children or put an end to unnecessary and expensive tests. "It is our contention that all patients with autism should be offered a thorough diagnostic evaluation," Schaefer and Mendelsohn conclude.

Physician Fee Schedule Issues Remain in Flux

Unless Congress steps in, the 10.1% cut in Medicare physician fees under the sustainable growth rate (SGR) update formula will take effect July 1 of this year. Lawmakers late last year blocked the cut from starting January 1

and approved a 0.5% increase through June 30. But as the House and the Senate reassembled for the final session of the 110th Congress, significant issues about another fix are unresolved. Most importantly, how long should a fix be and how to pay for it? The Bush administration has signaled its opposition to any cuts in Medicare Advantage, so other Medicare providers, including hospitals, nursing homes, and home health agencies—even potentially, labs—could become cutback targets to pay for a physician fee fix.

Another issue is the choice of legislative vehicle used for a fix and possibly for other changes in Medicare payment policy. Will it be a separate Medicare bill, a fee-fix-only bill like the one enacted last year, or part of an omnibus budget reconciliation bill, which under Senate rules requires only a simple majority to pass.

For the College of American Pathologists, preventing another SGR cut and increasing fees is a top priority, along with extension of the "grandfather" protection under which independent labs are allowed to bill Medicare separately for the technical component of pathology services to hospital patients. This provision expired at the end of last year, but Congress extended it for six months, through June 30 of this year.

Meanwhile, under changes in work and practice expense values, pathology payments will decline by 2% overall in 2008. However, changes in some practice expense values will mean higher rates for the technical component of flow cytometry and most in situ hybridization services.

PAML Creates Division to Commercialize Lab IT Products

Pathology Associates Medical Laboratories (PAML; Spokane, WA) has spun off an independent operating division to commercialize a range of technologies to support and expand outreach laboratory testing business. Named Outreach Advantage, the division will be led by Mark Johnston, former chief information officer of PAML and a presenter at Washington G-2 Reports's LabCompete conference in February.

Outreach Advantage's products consist of the systems that PAML has built internally to support its operations and joint ventures. They include an integrated technology package to plan lab courier routes and track specimens; a platform to connect laboratory information systems to EMR systems and Web products; and a customer relationship management (CRM) tool.

"Each of the Outreach Advantage products and services has been tested and proven in daily laboratory operations," said Johnston. "The combination of the key pre- and post-analytic functions into an integrated technology suite is unique in the industry and will greatly improve outreach laboratory effectiveness."

PAML has also secured an exclusive sales distribution agreement with Maplewood Software (Spokane, WA) to market and sell an application to automate scheduling, credentialing, and competency verification activities in laboratory departments. In addition, PAML has entered into an agreement with ARUP Laboratories (Salt Lake City) to market the Outreach Advantage products through their sales and service organization.

GE Healthcare to Buy Whatman for Life Sciences Expansion

The healthcare division of General Electric (Fairfield, CT) has agreed to acquire Whatman, a London-based supplier of filtration products and technologies, for approximately $717 million, the company announced on February 4.

GE Healthcare will use the acquisition to expand its $1.3 billion life sciences business, which includes the Amersham business acquired in 2004, as well as tools and technologies for cellular, molecular, and protein-based analysis. The all-cash transaction is expected to close in the second quarter of 2008.

"Life Sciences is a key area of growth for GE Healthcare, and expanding our skill base and product offerings in this area supports our vision of helping our customers to diagnose and treat disease earlier," said GE Healthcare President and CEO Joe Hogan.

At this time, GE plans to run Whatman as a stand-alone business and retain CEO Kieran Murphy, the company said during a conference call announcing the acquisition. Whatman, which has 1,100 employees, has annual revenues of approximately $230 million.

CMS Gives Pathologists Incentives for Quality Reporting

Beginning this year, many pathologists are eligible for a boost in payment from the Centers for Medicare and Medicaid Services (CMS) under the 2008 Physician Quality Reporting Initiative (PQRI). Although the agency's pay-for-reporting program began last year, there were no quality measures for pathologists to report prior to Jan. 1, 2008, when two pathology measures pertaining to breast and colorectal cancer patients were added to the program.

Eligible PQRI participants who successfully report on quality measures applicable to their practice in 2008 can earn a bonus payment, which is subject to a cap of 1.5% of the total Medicare allowed charges attributed to their individual national provider identifier (NPI) number. The pathology quality measures are based on recommendations from the College of American Pathologists (CAP).

While pathologists who don't diagnose breast or colorectal cancer specimens will not be able to participate in this year's PQRI, the program has broader implications. CMS plans to rely heavily on quality reporting in the future to determine physician payments, according to Dennis Padget, president of DL-Padget Enterprises (Simpsonville, KY) and publisher of *Pathology Service Coding Handbook*.

"CMS's objective for the next year or two is simply to gather actual physician quality measurement data," Padget explained. "Once the agency has gathered sufficient data and experience, it will attempt to link quality performance to physician payment. There will likely be 'carrots' where a physician is paid more for above average quality, but there almost certainly will be 'sticks' whereby payment is reduced or eliminated altogether for poor quality."

IVD Stocks Slump 7%; Abaxis Drops 22%

The 19 stocks in the G-2 Diagnostic Stock Index dropped an average of 7% in the five weeks ended February 8, with 16 stocks down in price and three up. The S&P 500 has lost 8% so far this year, and the Nasdaq is down 12%.

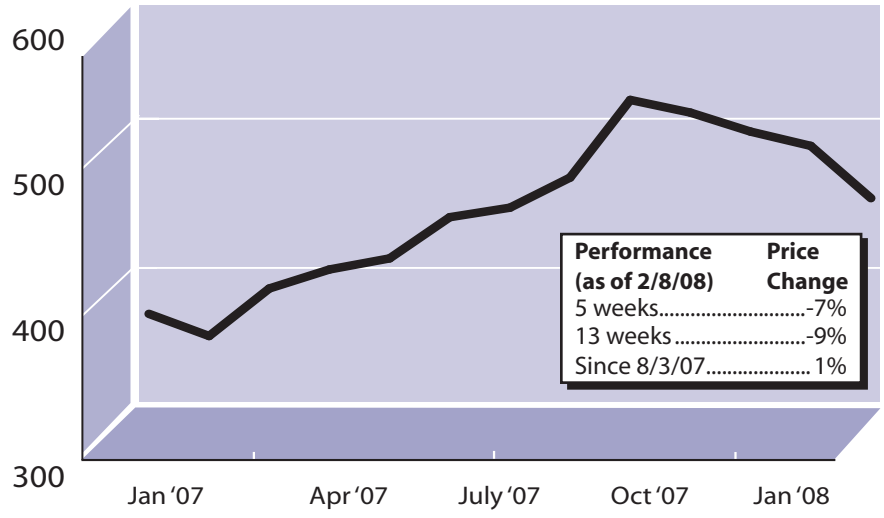
Shares in point-of-care blood test maker **Abaxis** (Union City, CA) were down 22% to $28.42 a share for a market capitalization of $630 million. On January 31, the company announced record revenue of $25.7 million for the third quarter of its 2008 fiscal year, but the results fell below Wall Street's estimates. On a conference call, CEO Clint Severson said that the greatest challenges of the period involved "timing and mix." The most significant of these hiccups was the timing of the regulatory approval for Abaxis's new Japanese distributor, Central Scientific Commerce, a subsidiary of Tokyo-based GSI Creos.

"Because the final approval was not received last quarter, we were not able to ship product to our new distributor in Q3," Severson said. This led to a 35% decrease in sales to the Pacific Rim region, a loss of about $351,000 compared to the same period last year. "With the approval we should be able to make this up over the next couple of quarters," he added. The Japanese authorities completed their inspection of the Abaxis facility in January, and the company expects the license to be issued in the current quarter.

For up to the minute laboratory and diagnostic firm data, financial news, and company podcasts—go to **www.g2reports.com**

Meanwhile, shares in molecular and rapid diagnostics company **Nanogen** (San Diego, CA) inched up to 0.45 per share for a market cap of $27 million. The company recently announced that Robert Saltmarsh, vice president and chief financial officer, will retire at the end of February. Taking his place is Nick Venuto, who previously served as executive director of finance. Nanogen also received two new patents in January. The patents, which cover nucleic acid amplification and fluorescent detection methods, add to Nanogen's approximately 40 existing patents in the field of real-time polymerase chain reaction (PCR).

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 19 IVD companies.

UP	Price	% Chg
Luminex	$16.97	2%
Nanogen	0.45	36
Ventana	89.47	2
DOWN		
Abaxis	$28.42	-22
Abbott Labs	56.80	-6
Affymetrix	19.45	-14
Beckman Coulter	70.49	-3
Becton Dickinson	89.95	-1
Bio-Rad	89.56	-9
Clinical Data	20.23	-2
Gen-Probe	56.94	-9
Immucor	27.16	-13
Inverness Medical	44.04	-27
Johnson & Johnson	62.03	-9
Meridian	31.11	-9
Nanogen	11.35	-19
OraSure	7.61	-14
Quidel	15.82	-5
Third Wave	8.02	-12

G-2 Insider

Business & Financial Strategies for Molecular Diagnostics: Making Dollars and Sense of Operating an MDx Lab . . . Learn how laboratories of various types and sizes are making molecular diagnostics work for them while getting the lowdown on regulatory and legal issues, building a molecular test menu, technical trends, personnel priorities, and more at Washington G-2 Reports's third annual molecular diagnostics conference. The meeting will take place from April 30 to May 2 at the Hyatt Regency in Cambridge, Massachusetts.

This lineup of experts and key topics includes:

- ❑ An opening keynote address by **Michael Laposata, M.D., Ph.D.**, who will address how clinical laboratories can harness the power of molecular diagnostics for meaningful growth.
- ❑ A regulatory overview and update by **Steven Gutman, M.D.**, director of the U.S. Food & Drug Administration's Office of In Vitro Diagnostic Device Evaluation and Safety.
- ❑ Sessions led by **Antonius Schuh, Ph.D.**, CEO of AviaraDX and **Gregory Critchfield, M.D.**, president of Myriad Genetics Laboratories, will explore the unique opportunities and challenges of personalized medicine.
- ❑ A look at how to best communicate molecular test results from Elaine Lyon, Ph.D., medical director of the molecular pathology laboratory at ARUP Laboratories

For more information, including a downloadable conference schedule and listing of program faculty, visit *www.g2reports.com*. To register, call G-2's customer service department at 1-800-401-5937, ext 2.

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