Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Roche to Acquire Remaining Stake in Genentech for $46.8 Billion

After a battle that stretched to nearly eight months, Roche (Basel, Switzerland) has sealed a friendly takeover deal with biotech company Genentech (South San Francisco, Calif.). The companies announced on March 12 that Roche will buy the 44 percent of Genentech that it doesn't already own in a deal valued at $46.8 billion, or $95 per share in cash. Another demonstration of Roche's commitment to personalized medicine-based health care, the deal is likely to ignite further biotech deal activity.

The combination of Roche and Genentech will create the seventh largest U.S. pharmaceutical company in terms of market share. Roche plans to operate research and early development activities as an independent center at Genentech's South San Francisco campus, where it will also relocate Roche's commercial pharma operations, currently based in Nutley, New Jersey. The combined company's U.S. commercial operations in pharmaceuticals will operate under the Genentech name, and the existing U.S. sales organizations of both companies will be maintained.

"Roche and Genentech saw the potential of a pharma-biotechnology partnership early on, and we are now in an enviable position to expand on the success of our longstanding relationship, which has been a source of immense value for patients, employees, and shareholders of both companies," said Roche CEO Severin Schwan. For more on Roche, see *Inside the Diagnostics Industry*, pp. 5-6.

Beckman Coulter to Buy Lab-Based Diagnostics Division From Olympus

After nearly 40 years, Olympus (Tokyo, Japan) has decided to exit the clinical diagnostics systems business. On February 27 the company announced that it has agreed to sell its diagnostics systems business to Beckman Coulter (Orange County, Calif.) in a deal valued at approximately $800 million. The business, which consists mainly of automated chemistry analyzers and automated blood transfusion systems, generated revenue of approximately $540 million in 2008.

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▲ **Beckman Coulter,** *from page 1*

Beckman has agreed to acquire the R&D, production, and marketing functions of Olympus's diagnostic systems business. As part of the agreement, Beckman can provide up to 37.5 percent of the purchase price in the form of its stock. The company also plans to finance the deal with a combination of newly issued common stock (approximately $300 million) and newly issued debt (approximately $500 million). The deal has a target closing date of July 1.

Olympus explained that the divestment stems from "the presence of several large existing competitors, an increase in M&A activity, and the entry in recent years of significant new players from other industries [that] have created a new competitive environment in this market segment."

The acquisition broadens Beckman's clinical chemistry offering, particularly in larger hospital laboratories. "In addition, the transaction will extend our broad chemistry customer base representing a valuable new customer set for Beckman Coulter's immunoassay products," noted Beckman in a statement announcing the agreement. The deal will make Beckman the third-largest player in the clinical diagnostics market, behind Roche and Siemens.

Beckman expects the Olympus business to provide revenues of approximately $500 million in 2010. Beckman reported 2008 revenue of $3.1 billion, up 12.2 percent over the previous year. Revenue from clinical diagnostics grew 13.5 percent in 2008 as compared to 2007, while sales in the company's life sciences division were up 6.1 percent.

In addition to planned savings of $50 million to $60 million from "leveraging existing global infrastructure and integrating sales, service, administrative, and R&D activities," Beckman plans to eliminate Olympus's immunoassay product line and the related R&D program after the deal closes.

SACGHS Issues Draft Report on Gene Patents

The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) has issued a draft report on gene patents and licensing practices and their impact on access to genetic tests. The committee is seeking public comment on the draft report. Comments are due by May 15.

The public consultation draft report is the result of work that began in 2004, when SACGHS identified the effects of gene patents and licensing practices on patient and clinical access to genetic tests as a high-priority issue that warranted further study.

The task force reviewed a number of case studies to draw conclusions about how gene patents affect pricing, access to and availability of genetic tests, innovations and research related to genes, and other areas. The case studies did not reveal "widespread overpricing" of genetic tests that were patented and exclusively licensed relative to those that are unpatented or nonexclusively licensed.

So far, the panel found, patents covering genetic tests and related licensing practices do not appear to be impeding patient or clinical access to tests. The report points out that in those cases where patient access was impeded, the problems tended to be caused not by the patent itself but by the way it was licensed or used.

"Concerns about the quality and validity of genetic tests may best be addressed by enhancing the oversight system for laboratory-developed tests," notes the draft report. At the same time, the panel observes, "If regulatory oversight of genetic tests evolves, requiring some type of costly independent review before marketing, patent protection may be needed for companies to be willing to risk resources in satisfying the regulatory requirements."

The report's final chapter provides a broad range of policy options for public consideration, including those focused on advocacy efforts by key stakeholders to ensure access to genetic tests, enhancing transparency in patents and licensing, filling data gaps, federal efforts to promote broad licensing and patient access, and improving United States Patent and Trademark Office policy.

Among the options presented for statutory change, which would apply to both the private and public sectors, are those that would limit the patenting of diagnostic tests that rely on an association of a particular genotype with a disease or disorder, create an exemption from patent infringement liability for medical practitioners who use genetic diagnostic tests in clinical care, and prohibit patents on human health-related nucleic acid sequences.

Enzo Biochem Buys Assay Designs for $12.2 Million

Life sciences and biotechnology company Enzo Biochem (New York City) has acquired privately owned Assay Designs (Ann Arbor, Mich.) for $12.2 million in cash, the companies announced on March 12.

With annual revenues of approximately $11 million, Assay Designs is a supplier to the biomedical, pharmaceutical, and scientific research markets. Its products include kits and reagents for the detection and quantification of small molecules and proteins that are important in inflammation and immunity, oxidative and cellular stress, steroid and hormone biology, and cell signaling.

The acquisition is a move to build Enzo's Life Sciences division, which develops, produces, and markets proprietary labeling and detection products for applications including gene sequencing, genetic analysis, and immunological research. Enzo Life Sciences revenues for fiscal 2008 totaled $35.7 million, accounting for 46 percent of Enzo's total company revenues, up from 24 percent in fiscal 2007.

In addition to complementary product lines, Assay Designs will provide Enzo with significant experience in protein, antibody, and immunoassay development and manufacturing. Enzo Biochem President Barry Weiner described the deal as evidence of the company's strategy "to position Enzo in the rapidly developing fields of scientific and medical research and diagnostics, where the practice of medicine is inevitably headed."

FDA Approves Hologic's HPV Tests

Hologic (Bedford, Mass.) has received premarket approval from the United States Food and Drug Administration (FDA) for both the Cervista HPV HR (high risk) and the Cervista HPV 16/18 tests. The tests are based on Invader chemistry, a patented molecular diagnostic technology acquired by Hologic through its July 2008 purchase of Third Wave Technologies.

Hologic's Cervista HPV HR test is designed to detect the 14 high-risk types of human papillomavirus (HPV) known to cause cervical cancer. It is the first HPV DNA test to be approved by the FDA since the agency's initial approval of Digene's pioneering Hybrid Capture 2 HPV DNA test in 1997. Cervista HPV 16/18 is the first HPV test approved for genotyping for HPV types 16 and 18, which are associated with approximately 70 percent of all cervical cancers in the United States.

The Cervista HPV HR test has been approved to screen patients with atypical squamous cells of undetermined significance (ASC-US) cervical cytology results to determine the need for referral to colposcopy and for adjunctive use with cervical cytology to screen women 30 years and older to assess the presence or absence of high-risk HPV types.

In women 30 years and older, the Cervista HPV 16/18 test has been approved for use with the Cervista HPV HR test in combination with cervical cytology to assess the presence or absence of specific high-risk HPV types. It is also approved for use with the Cervista HPV HR test in patients with ASC-US cervical cytology results.

Survey Finds Half of Labs Struggle With Hiring; Medical Technologist Vacancy Rate Tops 10%

The U.S. Department of Health and Human Services reports that by 2012, 138,000 lab professionals will be needed, but fewer than 50,000 will be trained.

Sixty-three percent of laboratories cite increased competition for qualified staff as the primary challenge for filling vacancies, according to the most recent Wage and Vacancy Study conducted biennially by the American Society for Clinical Pathology (ASCP; Chicago). Other hiring challenges include salary and job location. One-third of the 1,594 labs surveyed reported low compensation as a recruiting hurdle, while 28 percent said that job applicants were unwilling to relocate.

Respondents said that the most difficult positions to replace are medical technologists (MTs) at the staff level (63 percent) followed by medical laboratory technicians (MLT) at 38 percent. The highest vacancy rate was for MTs at 10.4 percent, primarily in the East North Central and Far West areas of the United States. Laboratory assistants (LA) also reported high vacancy rates at 8.8 percent; primarily in high-volume testing labs (26.3 percent). Histotechnicians (HT) also rated among the highest in vacancies at 8 percent. The survey showed MLTs with a 6.4 percent vacancy rate. MLT vacancies were highest in outpatient clinics, reference labs, and high-volume testing labs.

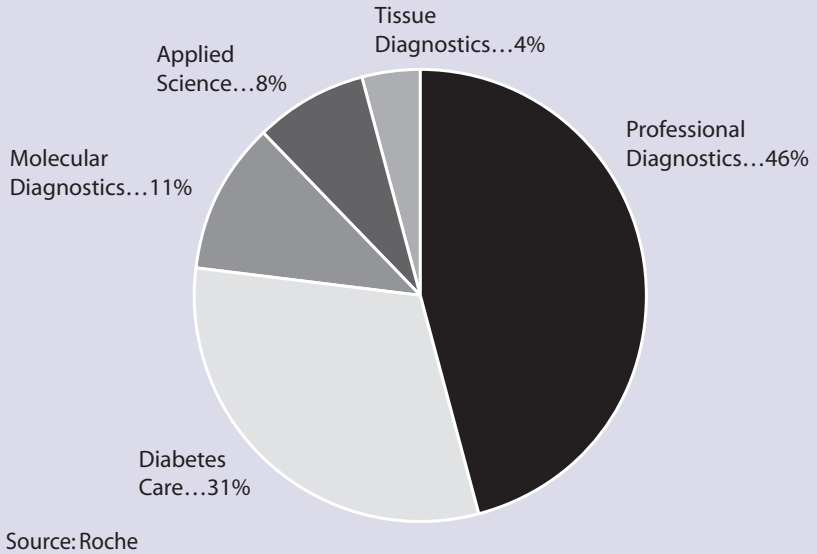
Roche Sees Double-Digit Diagnostics Growth in 2008

As many pharmaceutical companies look to enter new markets during the economic downturn, don't look for Roche (Basel, Switzerland) to diversify. At the group's annual general meeting in Basel on March 10, CEO Severin Schwan emphasized that Roche is focusing on its two core businesses: pharmaceuticals and diagnostics.

Roche is committed to improving drug efficacy and minimizing drug side effects through a personalized medicine approach that is rooted in diagnostics. "I believe that no other company in the world is better positioned to make personalized health care a reality. If you really want to tailor treatments to patients, you first need a good diagnosis," said Schwan, before highlighting recent acquisitions such as Ventana Medical Systems, which has allowed Roche to enter the area of tissue diagnostics. "We view tissue diagnostics as a major element in our efforts to tailor treatment to the needs of specific groups, particularly cancer sufferers," he added.

In 2008, Roche's total group sales increased by 6 percent in local currencies (-1 percent in Swiss francs; 10 percent in U.S. dollars) to CHF 45.6 billion (approximately $38.5 billion at current exchange rates), with the pharmaceuticals division representing 79 percent of group sales and the diagnostics division contributing 21 percent.

Roche Diagnostics: Revenue by Business Area



Source: Roche

The diagnostics division reported 2008 sales of CHF 9.7 billion (approximately $8.2 billion), a year-over-year increase of 10 percent in local currencies (3 percent in Swiss francs; 15 percent in U.S. dollars), outpacing the global in vitro diagnostics market's estimated 5 percent average annual growth.

Four of Roche Diagnostics' five business areas posted increased sales in 2008, with the largest gains coming from the professional diagnostics (up 9 percent in local currencies) and applied science (up 19 percent in local currencies) units. Key drivers of growth in these businesses were immunoassay systems and DNA sequencing products, respectively. In professional diagnostics, sales of clinical chemistry and immunoassay instruments grew by 10 percent, while immunoassay sales climbed 19 percent, led by tests for hepatitis C virus, NT

proBNP (N-terminal prohormone brain natriuretic peptide), and troponin T.

Sales in tissue diagnostics, the business area created through Roche's February 2008 acquisition of Ventana, have "exceeded expectations," according to Schwan, with growth exceeding 23 percent driven by immunohistochemistry and in situ hybridization instruments and reagents. The tissue diagnostics unit posted sales of CHF 376 million (approximately $317 million) in the 11 months through December 2008, accounting for 4 percent of the diagnostics division's annual sales.

Sales at Roche Molecular Diagnostics totaled CHF 1,122 million (approximately $948 million) in 2008, an increase of 5 percent over 2007. Growth in the business area, which accounts for one-third of the worldwide molecular diagnostics market, continues to be driven by virology testing. Demand was particularly high for automated real-time PCR platforms and tests for HIV-1, hepatitis C, and hepatitis B.

In the diabetes care area, sales were down 1 percent to CHF 3.0 billion (approximately $2.5 billion). Roche attributes the decline to flagging sales in the United States, where the second half of 2008 saw slowed sales of older glucose monitoring products, strong competition, and continued pricing pressures. Roche plans to launch four new diabetes monitoring products in 2009, including blood glucose meters targeted at younger patients and emerging markets.

Look for Roche's emphasis on personalized medicine and companion diagnostics to increase in the wake of its planned acquisition of U.S. biotech company Genentech (South San Francisco, Calif.), announced on March 12. Roche will buy the 44 percent of Genentech that it doesn't already own in a deal valued at $46.8 billion, or $95 per share in cash. "Working together, we aim to close the transaction quickly . . . allowing us to focus even more intently on innovation and long-term projects," said Roche Chairman Franz B. Humer in a statement announcing the deal agreement.

Roche plans to operate research and early development activities as an independent center from Genentech's South San Francisco campus, where it will also relocate Roche's Pharma commercial operations, currently based in Nutley, New Jersey. The combined company's U.S. commercial operations in pharmaceuticals will operate under the Genentech name, and the existing U.S. sales organizations of both companies will be maintained.

Meanwhile, on March 16, Roche announced that it has agreed to acquire innovatis (Bielefeld, Germany), a privately held company specializing in automated cell culture analysis, for 15 million Euros (approximately $19.5 million at current exchange rates). Focused on cell counting, viability testing, and cell function analysis, innovatis will be integrated into Roche Applied Science, a global business area of Roche's diagnostic division. The transaction is expected to close by the end of April.

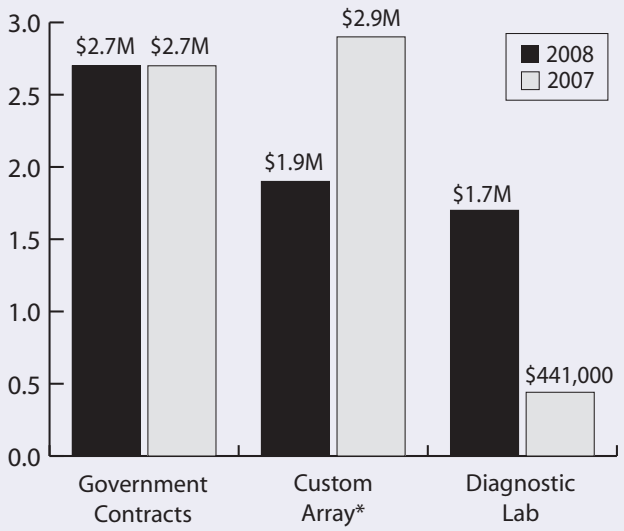
CombiMatrix Focuses on Increasing Test Utilization, Developing Cancer Screening Test

After a flurry of new product launches, biotechnology company CombiMatrix (Mukilteo, Wash.) will devote 2009 to increasing usage of its microarray-based diagnostic tests. The company is also moving ahead with the development of its Comprehensive Cancer Array (CCA) test, after reporting promising preliminary results that indicate the test can noninvasively and simultaneously screen for the early detection of prostate, colon, ovarian, breast, and lung cancers.

CombiMatrix recently reported 2008 revenues of $6.3 million, up five percent compared to 2007. The company's 2008 revenues were comprised of $2.7 million in government contact revenues; $1.9 million in CustomArray product, equipment, and service revenues; and $1.7 million in diagnostic lab revenues.

CombiMatrix Molecular Diagnostics (CMDX; Irvine, Calif.), the company's CLIA laboratory subsidiary, was a growth engine in 2008, with revenue from diagnostic services increasing four-fold over that of 2007. "Our diagnostic revenues continue to grow at a rate of between 25 percent and 50 percent, despite current economic conditions," said Amit Kumar, Ph.D., president and CEO of CombiMatrix, on a March 4 conference call with investors and analysts.

CombiMatrix Revenue by Segment



*Includes revenue derived from CustomArray products, equipment, and services.

Source: CombiMatrix

A portion of the growth in CombiMatrix's diagnostic lab revenues can be attributed to international sales of its microarray-based diagnostic tests, which the company initiated in 2008 and is looking to increase in 2009. In the fourth quarter of 2008, the company sold $63,000 worth of arrays for diagnostic use to laboratories outside of the United States. Because of the domestic regulatory environment, CombiMatrix does not sell its microarray-based diagnostic tests to other laboratories in the United States. It performs the testing itself in its CLIA-certified laboratory.

After launching at least one test per quarter in 2008, CombiMatrix will now focus on expanding the utilization of its current tests. "While 2007 and 2008 were the years of test development and launch, 2009 will be the year we seek to gain critical mass in utilization of our tests and correspondingly increasing revenue," said Kumar. "In 2008, more than 2,000 patients took our array-based tests. Our goal for 2009 is to more than double this

number and reach between 4,000 and 5,000 patients for the year. Already our laboratory is processing more than 300 patients per month."

Among the newly launched tests is ProScan, an array-based test for prostate cancer that CombiMatrix introduced last December through its CLIA lab. The ProScan test consists of probes for specific genomic loci of which copy number gains and losses have been shown to correlate with risk of recurrence and metastasis in patients post-prostatectomy.

"Our diagnostic revenues continue to grow at a rate of between 25 percent and 50 percent, despite current economic conditions."

Plans for boosting test utilization this year include expanding CombiMatrix's sales infrastructure by adding to its current staff of six salespeople and partnering with other laboratories. In 2008, CombiMatrix entered into a deal with molecular diagnostics laboratory Lenetix (Mineola, N.Y.) to co-market CMDX's suite of comparative genomic hybridization array-based tests. Continued publication of clinical studies is also expected to aid the company's marketing efforts.

"The challenge is getting the medical industry to accept [our tests]," said Kumar. "And that's happening. Every physician who orders a test for his or her patient becomes a recurring customer for us, but in the broader medical industry, physicians need to be educated on how to use these tests and what kind of benefits they can provide for their patients."

In commenting on the regulatory environment for molecular diagnostic tests, Kumar highlighted CombiMatrix's commitment to "be proactive and work with regulators to secure clear regulatory paths." The company has met with the United States Food and Drug Administration (FDA) and has "received a positive opinion regarding the operation of our tests under the regulatory guidelines of CLIA," noted Kumar. "To my knowledge, we're the only company that has received such an opinion in writing." In January, CombiMatrix announced that Scott Gottlieb, M.D., former deputy commissioner of the FDA, had joined its board of directors.

In 2008, CombiMatrix began developing its CCA test, which Kumar characterizes as "a game changer." Designed to be a noninvasive, comprehensive cancer screen, the test uses a blood sample "that can be drawn in concert with an annual physical," said Kumar. The test is focused on the five general cancers—prostate, colon, breast, lung, and ovarian—that comprise approximately 85 percent of the tumors diagnosed annually.

Unlike risk factor tests or tests designed to help select the best therapy, the CCA test is designed to screen for cancer and provide information to the patient and to the physician so that subsequent testing can be performed. CombiMatrix is continuing the research and development of the test and later this year plans to conduct internal validation trials.

Kumar estimates the number of candidates for the CCA test in the United States at 40 million to 50 million annually. The test could be used by the general population as

well as by those individuals with a family history of cancer and those who have been identified through other tests as having an elevated risk of developing the disease.

CombiMatrix aims to bring the CCA test to market as a CLIA test by mid-2010 but may introduce versions for a subset of the five cancer types sooner, depending on the results of clinical studies. "Our goal is to bring this test in, eventually, at about $250 or $300 per patient," said Kumar.

Finally, on March 12, CombiMatrix announced today that it had received a four-year, $858,298 contract from NASA's Ames Research Center to design and test a microfluidic system. The lab-on-a-chip instrument will incorporate CombiMatrix's semiconductor microarray as part of an integrated genetic analysis platform that can be deployed in satellites.

New Gene Associated With ALS Identified

An international research consortium has identified a novel gene for inherited amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease). This is the fourth gene associated with familial forms of the progressive neurodegenerative disease. Two papers, published in the Feb. 27 edition of *Science*, report mutations in FUS/TLS, a gene known to play a role in DNA repair and the regulation of gene expression. The mutations affect the behavior of the FUS/TLS protein within cells and lead to deposits of abnormal protein within motor neurons.

The first study, led by researchers at Massachusetts General Hospital (Boston), found a series of 13 mutations in FUS/TLS, a gene that interacts with biological pathways already implicated in ALS and other neurological diseases, resulting in familial ALS of differing inheritance patterns and varying severity. Most cases of ALS are sporadic, with no evidence of inheritance, but 10 percent of cases appear to be inherited.

The researchers sought to validate their early data implicating FUS/TLS mutations by asking researchers at King's College London to screen the families they had been studying. The KCL team reported three mutations in eight apparently unrelated families and went on to characterize the effect of the mutations in cultured cells. They also identified deposits of FUS/TLS protein in motor neurons of three patients with FUS/TLS mutations, deposits absent from patients with other mutations or sporadic ALS.

The MGH-led team then analyzed brain tissue from one of its patients and also found abnormal deposits of the FUS/TLS protein in the nucleus of both neuronal and non-neuronal cells, along with degenerative changes typical of ALS.

"We've just begun to look at how these apparent FUS/TLS aggregates relate to the disease process—whether they contribute to neuronal damage or protect against it," said Thomas Kwiatkowski, M.D., Ph.D., of the MassGeneral Institute for Neurodegenerative Disease, lead author of the first study. "We're also developing a genetic test for mutations in this gene, which could help screen at-risk individuals and aid clinicians in diagnosis."

DTC Advertising, Expanded Salesforce Drive Myriad's Q2 Revenues Up 58%

Salt Lake City-based Myriad Genetics's second quarter 2009 molecular diagnostic revenues climbed 58 percent to $84 million, driven primarily by the company's strategy to penetrate the women's health diagnostic testing market. Myriad recently expanded its ob/gyn salesforce to 100, bringing the company's total salesforce to 250.

Another component of Myriad's sales strategy is its current $8 million physician and direct-to-consumer marketing campaign in Texas and Florida, promoting its BRACAnalysis test, which assesses a woman's risk of developing breast or ovarian cancer based on detection of mutations in the BRCA1 and BRCA2 genes. This campaign follows a successful outreach effort in the Northeast, and a Midwest campaign is also planned for 2010.

Like the current campaign, the expected investment for each effort is $8 million, according to Gregory Critchfield, president of the company's molecular diagnostic division, Myriad Genetic Laboratories. The company's pharmaceutical division is currently being spun-off from the parent company. The spin-off is expected to be completed by the end of this fiscal year, in July.

Critchfield sees tremendous potential in this ob/gyn testing market, particularly with regard to testing patients for BRCA mutations. An estimated one million individuals in the United States have BRCA mutations, but after 12 years of testing, only 4 percent have been identified. "The majority of individuals with mutations have not presented, and that's a very large market segment," he explained. Myriad is also marketing three other tests to the ob/gyn market (*see box*).

Myriad's Women's Health Test Menu

- ***BRACAnalysis:*** Assesses risk of developing breast or ovarian cancer based on detection of mutations in the BRCA1 and BRCA2 genes.
- ***Colaris:*** Assesses risk of developing colorectal and uterine cancer. COLARIS detects disease-causing mutations in three genes, MLH1, MSH2, and MSH6, which are responsible for the majority of hereditary nonpolyposis colorectal cancer.
- ***Colaris AP:*** Assesses risk of developing hereditary colorectal polyps and cancer by detecting mutations in the APC and MYH genes.
- ***Melaris:*** Assesses risk of developing melanoma through detection of p16 gene mutations, which occur in up to 40 percent of families with hereditary melanoma.

In addition to these sales and marketing efforts, reimbursement is an important aspect of Myriad's growth. Over 2,500 insurance plans now cover BRACAnalysis testing, and approximately 96 percent of Myriad revenues come from third-party payers. In addition, the average out-of-pocket test expense for most insured individuals is $50.45, so the cost is minimal to the patient. "Most people are willing to pay $50 for a test that is potentially life saving," said Critchfield.

Protein Shows Promise as Breast Cancer Biomarker

A small protein called lipocalin 2 (Lcn2) promotes breast cancer progression and when measured in tissues and urine, it can predict a cancer's invasiveness, according to a study conducted in the laboratory of Marsha A. Moses, Ph.D., at Children's Hospital Boston and published in the March 10 issue of the *Proceedings of the National Academy of Sciences*.

Tumors that are about to metastasize go through a process known as the epithelial to mesenchymal transition (EMT), which also occurs during normal embryonic development. Tumor cells revert to a less-differentiated state, stop adhering to each another, and become more mobile and prone to invade and multiply.

Researchers induced human breast cancer cells to make large amounts of Lcn2 and showed that cell motility and invasiveness increased significantly. They then took cells from aggressive breast cancers and silenced Lcn2 and found that cell migration was significantly inhibited. When they transplanted human breast cancer cells into animals, those from tumors making Lcn2 were more locally invasive and more likely to metastasize to lymph nodes.

A new study demonstrates that Lipocalin 2, previously associated with estrogen receptor-negative breast tumors, promotes breast cancer progression and may be a useful biomarker of the disease.

Further studies indicated that Lcn2 decreases the levels of estrogen receptor alpha. This reduces the cells' response to estrogen, which is associated with poor prognosis of breast cancer.

Finally, immunohistochemistry studies demonstrated Lcn2's potential as a tissue biomarker of human breast cancer. The researchers also found that increased levels of Lcn2 in the urine of women with metastatic breast cancer suggested that Lcn2 may have potential as a noninvasive biomarker for advanced breast cancer.

Lcn2, along with other urine biomarkers identified in Moses's lab, has been licensed to Predictive Biosciences (Lexington, Mass.) for clinical development.

NEJM Study Shows IHC Test Identifies Heart Condition

A new immunohistochemical test is reliable in diagnosing a serious arrhythmic heart condition known as arrhythmogenic right ventricular cardiomyopathy (ARVC), according to a study published in the March 12 issue of the *New England Journal of Medicine*. The findings offer the possibility of a highly sensitive and specific way to identify this life-threatening condition at an early stage, when it can be treated by implanting a cardiac defibrillator.

"ARVC has been linked to genetic mutations in proteins that form desmosomes, subcellular structures responsible for cell-to-cell adhesion," explains the study's

Affecting approximately one in 5,000 people worldwide, ARVC is associated with ventricular arrhythmias and sudden death. The hereditary condition often has no symptoms or warning signs.

senior author Jeffrey E. Saffitz, M.D., Ph.D., chairman of the department of pathology at Beth Israel Deaconess Medical Center (BIDMC; Boston, Mass.) and professor at Harvard Medical School. Several years ago, he and his colleagues discovered that a desmosomal protein known as plakoglobin was dramatically diminished in tissue samples of ARVC. In this new study, the authors examined if this reduced plakoglobin signal could serve as a biomarker for ARVC early in the course of the disease.

After ascertaining that the protein was indeed diminished in cases of ARVC—and not from other types of heart disease—they performed "blinded" immunohistochemical analysis of heart-biopsy samples. The results were remarkably accurate. "On the basis of clinical criteria, we made the correct diagnosis in 10 of 11 subjects with definite ARVC and correctly ruled out ARVC in 10 of 11 subjects who did not have the condition," explains Saffitz. "There was no question that the plakoglobin signal level was reduced diffusely in the ARVC samples."

Previous studies have found that magnetic resonance imaging, electrocardiography, and echocardiography can accurately identify patients with advanced ARVC, these tests are much less sensitive for patients with earlier or less conspicuous disease.

"An immunohistochemical test [based on plakoglobin levels] could, in the future, provide clinicians with an important new diagnostic tool," he adds. "Cardiologists at major medical centers in the U.S. routinely evaluate cases of unexplained arrhythmias, and this new test may help them to identify ARVC in some of these patients and to exclude it as a cause of arrhythmias in others."

The researchers are now working to validate the new test, and BIDMC has filed patents covering methods of diagnosing ARVC.

FDA Launches Collaborative Nanotechnology Initiative

A new collaborative initiative among the U.S. Food and Drug Administration (FDA), the Alliance for NanoHealth (ANH; Houston), and its eight member institutions will work to accelerate the development of safe and effective medical products in the emerging field of nanotechnology, which involves the creation and use of materials at the level of molecules and atoms and presents challenges and opportunities for the FDA's regulatory jurisdiction, from food to medical devices to therapeutics.

According to an agreement announced March 10, the FDA/ANH Nanotechnology Initiative will work to expand knowledge of how nanoparticles behave and affect biologic systems and to facilitate the development of tests and processes that might mitigate the risks associated with nanoengineered products. All outcomes from this public-private partnership, an example of the FDA's Critical Path Initiative, will be placed in the public domain.

The ANH eight member institutions are Baylor College of Medicine, the University of Texas M.D. Anderson Cancer Center, Rice University, the University of Houston, the University of Texas Health Science Center at Houston, Texas A & M Health Science Center, the University of Texas Medical Branch at Galveston, and the Methodist Hospital Research Institute.

deCODE Genetics Receives California Clinical Laboratory License

Iceland-based deCODE Genetics has received a clinical laboratory license from the state of California for its CLIA-certified genotyping laboratory. Since April 2007, the facility has processed deCODE's DNA-based reference laboratory tests, including those that detect genetic risk factors for type 2 diabetes, atrial fibrillation, and myocardial infarction, as well as the company's deCODEme direct-to-consumer genome scans. The license allows deCODE to accept samples from California residents.

Kari Stefansson, CEO of deCODE, describes his company as unique for its focus on both biomarker discovery and bringing to market diagnostic tests. "Our competitors outsource the science, the DNA-analysis, or both," says Stefansson. "But for us this is the real foundation of personalized medicine, and we are committed to delivering only the best validated tests and the highest-quality results, all in-house."

Through its reference laboratory service, deCODE offers DNA-based tests for assessing individual risk of heart attack, type 2 diabetes, stroke, breast cancer, prostate cancer, and glaucoma. The company's deCODE diagnostic tests and deCODEme scans detect single nucleotide polymporphisms (SNPs) that are validated in large-scale studies.

PSA Levels Predict Prostate Cancer Risk in African American Men

Prostate-specific antigen (PSA) levels appear to be more predictive of a three-year prostate cancer risk in African American men compared to Caucasian men with a family history of prostate cancer, according to a paper published in the March issue of *Cancer Prevention Research*.

"It was previously thought that PSA levels were just naturally higher in African American men, suggesting a need to possibly adjust the threshold upward before recommending a biopsy," said Veda Giri, M.D., director of the Prostate Cancer Risk Assessment Program (PRAP) at Fox Chase Cancer Center (Philadelphia, Penn.).

Giri and researchers at the University of Chicago observed 646 high-risk men, of whom 63 percent were African American, in the PRAP, which is focused on aggressive early detection.

No "race specific" differences in PSA levels were found when race was measured using genetic markers of ancestry or the reports of participants. The researchers then analyzed men with a PSA between 1.5 to 4 ng/mL and who had at least one follow-up visit. They found that among men with a family history of prostate cancer, PSA levels had the same predictive value whether the men were Caucasian or African American.

These findings are unique in that typically men are not recommended for a prostate biopsy until their PSA levels rise above 4 ng/mL. Large-scale studies with longer follow-up are needed to confirm these findings. The authors also plan to conduct follow-up studies on outcomes from prostate cancer treatment to assess biochemical recurrence after radical prostatectomy versus radiation therapy, distant recurrence, quality of life after treatment, and death from prostate cancer.

Quest Acquires Rights to Prostate Cancer Biomarker

Quest Diagnostics (Madison, N.J.) has entered into a nonexclusive licensing agreement with Epigenomics (Berlin, Germany, and Seattle) to acquire the rights to one of the cancer-focused molecular diagnostics company's proprietary biomarkers, the companies announced today. The agreement gives Quest rights to GSTP1, a DNA methylation biomarker, to develop and commercialize a molecular-based laboratory-developed test to aid in the diagnosis of prostate cancer. Financial terms of the deal were not disclosed.

Several studies have demonstrated that methylated DNA of the GSTP1 gene in tissue may indicate the presence of prostate cancer. A test that detects the DNA methylation of GSTP1 in tissue biopsies in combination with conventional histopathology may improve the accuracy of prostate cancer diagnosis, particularly in cases with suspicious but inconclusive histology findings or patients with elevated PSA but repeatedly negative biopsies.

Last year, Quest licensed rights to use mSEPT9, Epigenomics' colorectal cancer biomarker, to develop and validate a blood-based laboratory-developed test as an aid in the detection of colorectal cancer.

MedPAC Would Link Payment Increase to Quality

Medicare Payment Advisory Commission recommendations would provide hospitals with a full payment update in 2010 for inpatient and outpatient services as a reward for better performance on quality measures, according to MedPAC's annual report to Congress.

MedPAC's March 2009 report states that while payments for hospital services were adequate in 2007, Medicare margins remained low and are expected to continue to fall. The report, released Feb. 27, found that efficient hospital providers roughly broke even on Medicare payments and costs and that a payment increase based on a quality incentive program was needed.

The commission first discussed the recommendation at its December 2008 meeting and finalized the recommendation to Congress with a unanimous vote Jan. 8.

The pay-for-performance program would vary payment increases based on quality-of-care data. While hospitals overall would receive the full marketbasket update, the increase to individual facilities would be greater than or less than the marketbasket level, depending on quality, the report said.

The report's recommendations aim to improve the efficiency of the Medicare program, which MedPAC Chairman Glenn Hackbarth wrote "is unsustainable over the long term." Hackbarth wrote in the report that Medicare spending per beneficiary has been increasing over 2 percent a year faster than gross domestic product for the last 30 years.

"At this rate of increase, there is risk that Medicare will effectively crowd out spending on many important public programs, including those vital to preserving and enhancing the nation's health," Hackbarth wrote.

IVD Stocks Plummet 21% as Markets Falter

After two consecutive months of gains, the 17 stocks in the G-2 Diagnostic Stock Index fell an average of 21 percent in the five weeks ended March 6, with all 17 stocks down in price. So far this year, the G-2 index has fallen 17 percent, while the Nasdaq is down 18 percent and the S&P 500 has plummeted 23 percent.

Usually steady **Meridian Bioscience** (Cincinnati) was caught in the market's sharp downturn, falling 20 percent to close at $17.86 per share with a market capitalization of $743 million. In February, the company received clearance from the U.S. Food and Drug Administration for a new test for Campylobacter bacteria. Known as Premier Campy, the rapid test can be used to detect the most commonly diagnosed bacteria for food borne illness in the United States.

Shares in **Nanogen** (San Diego), slipped 12 percent to a March 6 closing price of $0.15 and a market capitalization of $10 million. According to the company's recently released preliminary financial results, total revenues for 2008 reached $46.9 million, an increase of 23 percent from the prior year. The cash-poor company is looking for a buyer. "We are aggressively continuing our efforts with Cowen & Co. to identify and evaluate strategic opportunities for our business," said Chairman and CEO Howard Birndorf in a statement issued along with the unaudited financial results. "This effort is one of our highest priorities."

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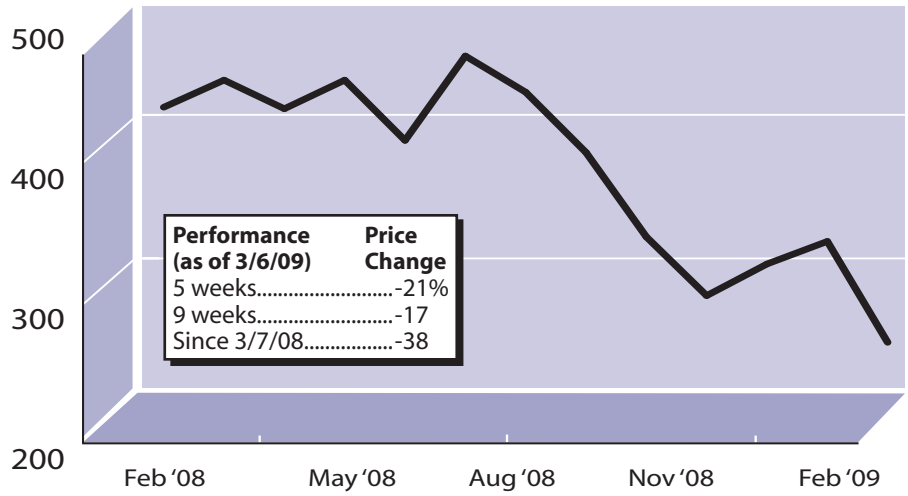
On March 4, Nanogen announced that it will license its proprietary minor groove binder (MGB) Probe technology to Quest Diagnostics (Madison, N.J.). Under the licensing agreement, Quest will have rights to use and sell products and services that incorporate the MGB Probe technology. Terms of the agreement include an upfront fee and royalties paid on tests sold using the licensed technology. Nanogen's MGB Probe technology is broadly licensed in the research and clinical fields and accounts for a majority of the company's revenue.

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 17 IVD companies.

Down	Price	% Chg
Abaxis	$16.14	-14%
Abbott Labs	46.89	-18
Affymetrix	1.89	-46
Beckman Coulter	41.67	-17
Becton Dickinson	64.15	-13
Bio-Rad	54.97	-19
Clinical Data	7.79	-21
Gen-Probe	40.08	-14
Immucor	21.02	-26
Inverness Medical	21.97	-12
Johnson & Johnson	47.97	-18
Luminex	15.66	-24
Meridian	17.86	-20
Nanogen	0.15	-12
Nanosphere	3.04	-37
OraSure	2.32	-17
Quidel	9.55	-29

G-2 Insider

Learn how to make outreach testing work . . . Washington G-2 Reports' and Chi Solutions' 2009 Lab Outreach Conference will focus on how to maximize value, profitability, and service through a slate of session topics that include using blended lab/imaging programs for outreach growth, managing outreach clients in the managed care environment, and developing a sustainable financial model for building outreach profitability. The premier business event dedicated to improving group, hospital, and health system laboratory outreach programs will take place June 8-10 at the Hyatt Regency Mission Bay Spa and Marina in San Diego. Among the confirmed speakers and sessions:

- ❑ **Michael Metzler,** the former COO of St. Elizabeth's Medical Center, and CEO of St. Anne's Hospital, will give a keynote presentation entitled "Know Your Numbers": What You Need to Know About Outreach From a CEO Perspective;
- ❑ **Leslie Wainwright, Ph.D.,** senior vice president at Sg2, will look ahead in a second keynote presentation, "Health Care 2020";
- ❑ Chi Solutions President **Kathy Murphy, Ph.D.,** will provide an exclusive overview of the eighth *National Outreach Survey*, including the five top industry trends; and
- ❑ **Ilke Panzer,** vice president of diagnostic laboratories at the Blood Center of Wisconsin, will discuss "Optimizing Your Test Menu: How a Carefully Designed Molecular Diagnostic Offering Can Impact Your Bottom Line."

For full program details, visit *www.g2reports.com/outreach09*. To register, call John Watkins at 800-401-5937 ext. 4710 or e-mail John at johnwatkins@ioma.com.

Company References

Alliance for NanoHealth 713-500-2466
ASCP 312-541-4999
Assay Designs 734-668-6113
Beckman Coulter 800-742-2345
CombiMatrix 425-493-2000
DeCODE Genetics 354-570-1900
Epigenomics 49-30-24345-0
Enzo Biochem 212-583-0100
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