Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Stephanie Murg, Managing Editor, smurg@ioma.com

Vol. VIII, No. 11/July 2008

CONTENTS

WASHINGTON G-2 REPORTS

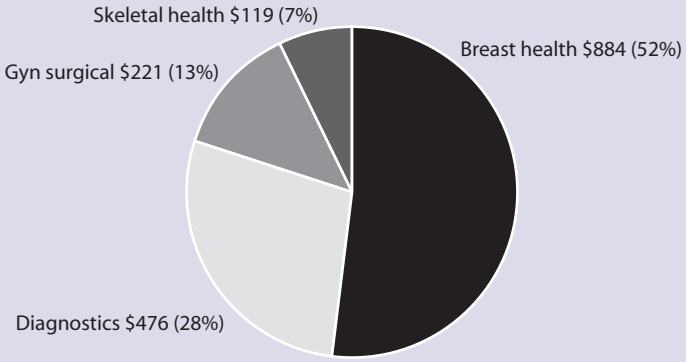
Established 1979

www.g2reports.com

Hologic to Enter Molecular Diagnostics With Third Wave Buy

Hologic (Bedford, Mass.) is entering the molecular diagnostics market. The women's health-focused company has agreed to acquire molecular diagnostics company Third Wave Technologies (Madison, Wis.), known for its proprietary Invader test platform. The purchase price of $11.25 per share, or approximately $580 million, represents a premium of about 24 percent to Third Wave's average trading price over the last three months. The transaction is expected to be completed in the third quarter of this year.

Hologic FY 2008 Revenue* *(in millions)*



Total Revenue: $1.7 billion

*Forecast as of June 9, 2008. Hologic's fiscal year-end is the last Saturday in September.

Source: Hologic

Hologic, which last year acquired ThinPrep Pap test maker Cytyc for $6.2 billion, stands to substantially expand its in vitro diagnostic test offerings, notably its cervical cancer screening business. In April, Third Wave submitted to the FDA its two molecular tests for human papilloma virus (HPV): a 14-type HR screening test (Cervista HR) and a type 16/18 genotyping test (Cervista 16/18). Earlier this year, the company received FDA clearance for its cystic fibrosis genotyping test. *Cont., on p. 2*

Veridex to Acquire Assets of Immunicon in Wake of Bankruptcy

Johnson & Johnson-owned Veridex (Raritan, N.J.) has agreed to acquire the assets of Immunicon (Huntingdon Valley, Pa.) for $31 million in cash, plus the release of certain claims owed to Veridex and the assumption of certain liabilities. A developer of proprietary cell- and molecular-based diagnostic and life science research products, Immunicon filed for Chapter 11 *Cont., on p. 2*

Hologic plans to initially focus on molecular tests for HPV, HCV, CT/NG, MRSA, and pharmacogenetics.

▲ Hologic to Enter Molecular Diagnostics, *from page 1*

In a June 9 conference call to discuss the Third Wave deal with analysts and investors, Hologic Chairman and CEO Jack Cumming called the molecular diagnostics market "a growing and important market that will impact the lives of people worldwide" and noted that Hologic had long been evaluating the area given the adjunct relationship of HPV testing to the company's ThinPrep Pap testing franchise.

"If and when Third Wave's HPV tests receive FDA approval, expected sometime in the first half of calendar 2009, we will be well-positioned to take these products quickly and effectively to market," said Cumming of the tests that would represent a direct competitor to that of Digene, which is now owned by Qiagen. "We believe that when fully commercialized, Third Wave's [HPV] assays will provide a competitive alternative to existing HPV tests due to its internal control that should reduce false negatives, the small volume of patient sample required to run the test, and the operational improvements afforded to the lab."

The deal would also give Hologic a novel platform for molecular diagnostics. The company noted in a statement that Third Wave's patented Invader chemistry "provides an exciting platform to explore new diagnostics for women's health." Cumming said that "with Third Wave, Hologic will be able to effectively compete in all segments of the molecular diagnostics market," although the initial focus will be on HPV, hepatitis C, Chlamydia/gonorrhea, methicillin-resistant *Staphylococcus aureus*, and pharmacogenetics. Third Wave's current clinical diagnostic offerings consist of products for such conditions as cystic fibrosis, hepatitis C, and cardiovascular risk.

Founded in 1986 by former CEO and Chairman S. David Ellenbogen and Chief Technical Officer Jay A. Stein, Ph.D., Hologic forecasts FY 2008 revenue of $1.7 billion, with over half of that ($884 million) coming from sales of breast health products and the balance derived from diagnostics ($476 million), surgical gynecology products ($221 million), and skeletal health products ($119 million).

▲ Veridex to Acquire Assets of Immunicon, *from page 1*

bankruptcy on June 11. Since 2000, Immunicon and Veridex have partnered to develop and commercialize novel cancer diagnostic platforms and products.

Founded in 1983, Immunicon's products include its CellTracks system and ferrofluid-based reagent kits designed to capture, count, and characterize rare cells in blood. The company's CellSearch circulating tumor cell (CTC) kit, marketed by Veridex, was Immunicon's first in vitro diagnostic product. The first diagnostic test to automate the detection and enumeration of CTCs, CellSearch is cleared by the FDA for the prognosis and monitoring of patients with metastatic breast, metastatic colorectal, and metastatic prostate cancer.

The assets to be sold by Immunicon include intellectual property, product inventory, and preclinical data, as well as all technologies related to the CellSearch system. Immunicon will also sell to Veridex all technologies related to the

company's Repeat-Free (RF) Poseidon fluorescent in situ hybridization (FISH) probes, a portfolio of 250 probes that offer faster hybridization with enhanced signal to noise ratio.

In addition to CellSearch assays, Veridex currently markets cancer molecular diagnostic tests under the GeneSearch brand. Its GeneSearch breast lymph node assay is the first-FDA approved molecular diagnostic assay for breast lymph node testing. Veridex plans to expand the GeneSearch product platform with additional gene-based diagnostic, confirmatory, and prognostic oncology tests for breast and other cancers.

President Signs GINA Into Law

On May 21, President Bush signed the Genetic Information Nondiscrimination Act (GINA), enacting the anti-discrimination measure that was broadly embraced in Congress. GINA prohibits employers and health insurers from discriminating against individuals based on their genetic information and test results. Bush praised the bill for protecting "our citizens from having genetic information misused . . . . without undermining the basic premise of the insurance industry."

The new law prohibits insurers from denying coverage to an individual or charging that person higher premiums based solely on a genetic predisposition to developing a disease. The legislation also bans employers from using an employee's genetic information when making hiring, firing, job placement, or promotion decisions.

"Individuals no longer have to worry about being discriminated against on the basis of their genetic information, and with this assurance, the promise of genetic testing and disease management and prevention can be realized more fully," said Sharon Terry, CEO of Genetic Alliance and president of the Coalition for Genetic Fairness.

The American Clinical Laboratory Association called GINA "a vote for the future." President Alan Mertz said in a statement, "Genetic testing is already making great strides in cancer, HIV, heart disease, and other areas—and this is just a start."

GINA received overwhelming support in both the Senate, where it was approved by a unanimous vote, and the House of Representatives, where the legislation was passed by a vote of 414-1.

A majority of states have laws to protect the public from genetic discrimination, and they vary widely in approach, application, and level of protection. While GINA establishes uniform national safeguards, it does not preempt state requirements.

Nanogen to Develop Flu Test for CDC

In vitro diagnostics company Nanogen (San Diego, Calif.) has been awarded a new $10.4 million, two-year contract from the U.S. Centers for Disease Control and Prevention (CDC) to develop a multi-analyte molecular diagnostic assay for

influenza. According to the contract, the rapid molecular test is to simultaneously detect and differentiate among Influenza Type A, Influenza Type B, seasonal flu (H1N1 and H3N2) strains, and Respiratory Syncytial Virus (RSV). The contract also provides for a secondary, "reflex," test for avian flu strains (H5N1, H7N1, and H9N1) for samples that are determined to be positive for Flu A but negative for seasonal flu.

Nanogen will develop the molecular diagnostic test in partnership with the Medical College of Wisconsin (MCW; Milwaukee, Wis.) and HandyLab (Ann Arbor, Mich.). The company expects that it will be significantly more sensitive than current rapid flu tests and will provide results in less than half the time it takes to run current molecular tests.

By 2010, the worldwide influenza diagnostics market is expected to reach $200 million.

In developing the new test, Nanogen will incorporate the company's ongoing collaboration with MCW as part of a National Institutes of Health grant for multiplexed infectious disease diagnostics. The proposal to the CDC included the use of Nanogen's proprietary probe technology for real-time PCR and anticipates the use of off-the-shelf instrumentation for sample handling and detection, including HandyLab's Raider microfluidic real-time PCR platform.

This is Nanogen's second CDC contract related to the development of diagnostic tests for influenza and complements the rapid test currently being developed by the company in collaboration with HX Diagnostics (Emeryville, Calif.).

Innovative Biosensors Raises $11.5 Million

Rapid detection developer and manufacturer Innovative Biosensors (IBI; Rockville, Md.) has closed on a $9.5 million Series B round of equity funding led by Life Sciences Partners, IBI announced on May 20. Other funders include Harbert Venture Partners, Chart Venture Partners, and New Markets Growth Fund. IBI also secured a $2 million increase to its debt facility, for a total of $11.5 million in debt and equity capital.

Privately held IBI has commercialized its proprietary BioFlash biosensor technology for the environmental detection of biothreat pathogens and is now developing the technology in a clinical instrument format beginning with the detection of infectious diseases.

Last month, IBI announced that it will collaborate with nonprofit biological resource and research organization ATCC (American Type Culture Collection) to develop a rapid, portable test to detect Avian (H5N1) influenza virus. ATCC will provide its monoclonal antibodies to H5N1 to IBI, which will develop the test on its biosensor-based platform.

IBI's initial funding round of $6.25 million was completed in October of 2006.

Special Focus: Genetic Testing

In this special supplement to DTTR, we focus on some recent developments and key players in the rapidly evolving world of genetic testing. With genetic tests now available for over 1,500 diseases and conditions, this onetime niche market of the in vitro diagnostics industry is playing an increasingly valuable and prominent role in health care, from assisting clinicians in the management of diseases and in the selection of treatment to enabling earlier diagnosis and prediction of disease risk years before symptoms occur.

It seems that each week brings newly published findings of disease-linked genetic variations, and here we highlight recent studies that enrich our understanding of the genetic influences in lung cancer and Alzheimer's disease. At the same time, there remains widespread concern over the best ways to develop, validate, use, interpret, and regulate this area of testing, and these issues were the focus of the June 12 roundtable convened by the Senate Special Committee on Aging and discussed on p. 7. In the meantime, as Human Genome Project leader Francis Collins told a congressional committee last year, "the science of genomic medicine is rocketing forward."

Under New CEO, Interleukin Genetics Looks to Educate Physicians and Consumers, Diversify Distribution

Founded in 1986, Interleukin Genetics (Waltham, Mass.) is best known for its DNA-based tests for genetic risk factors that affect inflammatory response. Today, as the company expands beyond tests for variations in its namesake interleukin-1 (IL1) gene, it is focused on three business areas: risk assessment testing through its CLIA-certified laboratory, non-pharmaceutical products such as nutritional supplements (through a partnership with consumer products company Alticor), and pharmaceuticals to treat disease. Now in the pipeline at Interleukin are weight management-related tests based on fat storage-linked single nucleotide polymorphisms (SNPs) licensed from Tufts University. Also in the research stage are tests for osteoarthritis and rheumatoid arthritis.

In January of this year, Interleukin named Lewis H. Bender as its new CEO. A biotechnology industry veteran, Bender spent 14 years as senior vice president of business development at Emisphere Technologies and briefly served as the company's interim CEO before joining Interleukin. *DTTR* recently talked with Bender about the company's past, present, and future.

Why did you decide to join Interleukin?

I think the personalized medicine field is on the verge of finally really making the impact that it should be. I think that it's critical to identify the patients most at risk for the diseases that are chronic in nature—where most of the health care costs go. These are heart disease, cancer, diabetes, osteoporosis, osteoarthritis, rheumatoid arthritis, and asthma. With these diseases, we're not talking about a patient population of 100,000 or 200,000, we're talking 10s of millions of people with these kinds of afflictions. I think if you could identify those people and get them preventative care, you would have a major impact on the way that health care would be treated.

At the end of the day, I just said that this is where I can make a major impact, and Interleukin has very good intellectual property on the diseases of inflammation, which are the chronic diseases, and so I just saw the opportunity to have an impact on health care.

Inflammation plays a complex role in disease. How do you address the challenge of educating physicians and consumers about it?

That's where the company I don't think has done an absolutely good job and hopefully where we come on board . . . . I think that there are a number of things that are important to do for

the education of both the physicians and the public, and the two audiences are somewhat different and somewhat the same. First of all, anybody who wants to obtain a genetic test, if they're a rational person, they're going to look at it with their health care provider, which is generally their doctor. So the consumer and the doctor are somewhat linked. Both of them are trying to do the same thing—prevent disease or help the person improve their health. And in order to do that, you need to have very good scientific quality in the types of tests and products that you create. So I think that the important thing is a good, scientific, rational, peer-reviewed publication approach that can allow people to have confidence that the data that you're generating is going to be valuable.

If you publish in a peer-reviewed journal, then clearly that is for the doctor. The main consumer is not really going to be sophisticated enough to understand the scientific, peer-reviewed publications. The problem is that doctors don't generally have the time to look at it, even if it's peer-reviewed, just because of their hectic schedules. So in that case, you need to be able to somehow bridge the patient and the doctor, with enough quality information, with enough quality science and references behind it to make sure that both the doctor can look it up if they're curious, but the patient and the doctor can both understand it without having to go into significant depth.

And how are you doing that?

It's a very delicate medical education process that's necessary. . . . And it's really a multi-pronged educational process—going to peer reviewed publications, getting key opinion leaders to sign off on the science, getting publications so that doctors can look at them, translating the information into a usable test report that goes to the consumer as well as the doctor, and getting the information clearly understood, and with the right references and the right science behind it so that once they read these multiple types of educational materials, they can get a very good, comprehensive understanding of the results of the test.

What is Interleukin's business model? How do the different pieces of the business—genetic tests, supplements, and pharma—fit together?

The business model that we have is to make sure that we have the reputable science, regardless of whether it's the pharma or the consumer side, with regard to the test, and that's number one. The marketing approach is to make sure the consumer is aware of the test, and that's where our partnership with [consumer products company] Alticor does very well.

Another one of the things that we want to make sure of is that if you do know the results of your test that there's something you can do about it. Let's say that you have a genetic risk for a certain disease that's fairly high—say an sixfold or eightfold or higher risk—well, if there's nothing you can do about it or there's nothing that can be done to change the course or progression of that disease from a risk point of view, why would you even bother getting the test? So there has to be some sort of guidance and solution that can be done in order to reap the most benefits from the results of the test.

We do that first of all by having genetic counseling available to people who purchase our tests, but . . . . the business that we have is to couple biomarkers and measured quantities of indicators *along with* the genetic risk to really give a person a way of controlling their risk.

Where does the supplements business fit in?

Our supplements business has nothing to do with our heart health test. It's just a way for us to be able to distribute the tests through the pharmacy channel. We have the access, we have the contacts at the pharmacies, and what we would like to get them to do is put on the shelf the

genetic risk tests, so that when the doctor wants it, the person can just go down to the pharmacy and get it.

That's one channel. We use the Alticor channel as another way of distributing the tests, and we're going to be going direct to consumer with other types of vehicles to distribute the tests. So our supplements business has nothing to do with our genetic tests. Our supplements business is really a way for us to generate cash so that we don't have to dilute shareholders as well as a distribution channel when we're ready to launch there and go to the pharmacy directly.

Interleukin opened its CLIA-certified laboratory in 2006. Is all of your testing done there?
Everything with the exception of a dental test [that analyzes two IL1 genes for variations that identify an individual's risk for periodontal disease] that we have outlicensed to a couple of firms on a nonexclusive basis that we get royalties from.

Can you give us any indication of the testing volume that you're seeing at the CLIA lab or the growth rate?
I'll give you the history. When this [CLIA lab] got launched, it was extraordinarily successful. In fact, we probably have done more genetic risk assessment tests than just about anybody—maybe Myriad [Genetics] has done more, it depends on what you define as genetic risk assessment. But we were selling 10s of thousands of these tests, and I think, to your first question, test sales have dropped off. They're between 500 and 1,000 per month right now, and I think that the reason that they've dropped off is due to the fact that we did not appropriately indicate what the results meant and what you do if you are genetically positive. And that's what we're in the process now of repairing.

At the same time, we didn't support our partner Alticor with the science by going around to the people who sell their products and explain to them what the benefits are of the tests. So their independent business operators sort of ceased selling the tests, because I don't think they really knew what the patients could do if they had a positive result. So we're changing all that—to communicate what the results mean, support it, know the science behind it, and get that information out to the people who are distributing these tests, as well as go around supporting those efforts to sell the tests.

Senate Aging Committee Convenes Roundtable on Genetic Testing

On June 12, Senator Gordon H. Smith (R-Ore.), ranking member of the Senate Special Committee on Aging, held a roundtable discussion of the regulatory, scientific, and ethical issues relating to genetic testing. Among the participants were Thomas Hamilton, director of the survey and certification group at the Centers for Medicare & Medicaid Services (CMS); Judy Yost, director of the division of laboratory services/CLIA program at CMS; Steven Gutman, M.D., director of the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety; and Kathy Hudson, Ph.D., director of the Genetics and Public Policy Center at the Johns Hopkins University.

"The roundtable presented an opportunity for Senator Smith to hear all sides of the genetic testing issue," American Clinical Laboratory Association (ACLA) President Alan Mertz told *DTTR* after the meeting. "What came through loud and clear was the value of genetic testing, the tremendous innovation occurring, the complexity of the issue, as well as the need for smart,

careful, and effective regulatory oversight that does not stifle innovation."

In her comments at the roundtable on behalf of ACLA, Elaine Lyon, Ph.D., associate professor of pathology at the University of Utah School of Medicine and medical director of molecular genetics at ARUP Laboratories (Salt Lake City), emphasized the clinical importance of genetic testing and addressed some misconceptions regarding its validation and regulation.

Lyon called for tests that are based on sound medical knowledge and ordered by a health care professional who is well-equipped to guide their proper use and interpretation. She went on to note that laboratories that perform these tests should be CLIA-certified for high complexity testing and called for exaggerated or unsubstantiated testing claims to be investigated by the Federal Trade Commission.

"Innovation in molecular testing is extremely sensitive to regulation and reimbursement," noted Lyon in closing. "Too much of the former and too little of the latter could prevent or delay the hoped-for medical advances. I believe we can target the problems of marginally useful testing while allowing testing based on good science to accomplish its promise of diagnosing, treating, and preventing disease."

Common Gene Disorder Found to Double Lung Cancer Risk

Alpha-1 antitrypsin deficiency (α1ATD), a common genetic disorder, doubles the risk of developing lung cancer for both smokers and nonsmokers, according to a study published in the May 26 issue of the *Archives of Internal Medicine*. Researchers from the Mayo Clinic found that α1ATD could explain up to approximately 12 percent of the 1,443 lung cancer patients in this study and likely represents the same widespread risk in the general population.

"[α1ATD] is a seriously underdiagnosed disorder and suggests that people who have lung cancer and chronic obstructive pulmonary diseases (COPD) in their families should be screened for these gene carriers," says Ping Yang, M.D., Ph.D., a Mayo Clinic epidemiologist and lead investigator of the study.

A normal α1ATD gene produces a protein that stops enzymes from breaking down elastin, which keeps lung tissue elastic for normal function. Carriers of α1ATD commonly develop emphysema and/or COPD. Prior to this study, the connection between α1ATD, COPD, and lung cancer risk had not been established.

"It has been suspected that α1ATD increased susceptibility to lung cancer," says Dr. Yang, "but this is the first solid evidence that supports and quantifies this risk."

The current standard diagnostic test for α1ATD measures protein produced by the gene. Because of its cost and limited availability, the test is not suitable for general screenings. A less expensive DNA-based gene panel test is being developed.

In this study, a team of researchers looked at three different groups: 1,443 patients with lung cancer treated at Mayo Clinic and two groups of controls, one of which consisted of siblings of the lung cancer patients. They found that the α1ATD carrier rate among the genotyped patients with lung cancer was 13.4 percent, compared to 7.8 percent among unrelated control participants.

All α1ATD gene carriers were at a similarly greater risk of developing lung cancer, regardless of smoking status. Those who had never smoked were at a 2.2-fold higher risk; light smokers had

a twofold greater risk; and moderate to heavy smokers had a 2.3-fold increased risk. A history of COPD increased lung cancer risk significantly for light, moderate, and heavy smokers, but affected those who had never smoked the most—an almost sixfold increased risk.

Increased lung cancer risk among α1ATD carriers is independent of a family history of lung or other cancers. The estimated attributable risk for α1ATD carriers in this study among those who never smoked and among heavy smokers was 11 percent to 12 percent, suggesting that the genetic disorder might explain a significant proportion of lung cancer in the general population. The majority of study participants were of European descent, the population in which this genetic disorder is most common.

Gene Variation Linked to Earlier Onset of Alzheimer's Symptoms

A study published in the June 10 issue of the *Proceedings of the National Academy of Sciences* has linked variations in the tau gene to an earlier presentation of Alzheimer's disease (AD) symptoms. Unlike genetic mutations previously linked to rare, inherited forms of early-onset AD, these variants affect those with the more common, late-onset form of the disease.

Researchers at the Washington University School of Medicine in St. Louis analyzed DNA from 313 subjects from the university's Alzheimer's Disease Research Center, focusing on locations in the tau gene that previously have been found to vary between people. This gene encodes the protein that comprises the neurofibrillary tangles that are one of the principal hallmarks of AD in the brain. Amyloid plaques, the other primary neuroanatomical feature of the disease, are made up of a protein called amyloid-beta.

"Some studies in the scientific literature show an association between the [tau] gene and Alzheimer's disease, while others do not," says principal investigator Alison M. Goate, D. Phil. "Even a study from our own group had found no association between tau gene variants and Alzheimer's disease." One reason past studies may have produced conflicting results is that most, if not all, people have amyloid plaques in the brain years before they develop clinical symptoms of AD.

Goate's team found that four DNA sequence variants in the tau gene were associated with higher levels of tau protein in the cerebrospinal fluid (CSF). Then they divided patients into two groups: those with evidence of plaques in the brain and those without. The researchers found that the gene variations are only associated with an increase in tau protein levels in CSF when there is evidence of amyloid plaques in the brain.

Going back to the DNA samples, they confirmed their assumption that individuals who carry these genetic variations that lead to higher levels of tau in CSF have an earlier age of onset than those who carry variants that are associated with lower levels of tau.

According to Goate, these sequence variants in the tau gene are not linked to risk of AD but rather to earlier cognitive problems once plaques have started to form in the brain. She says people who possess those genetic variants, if they are fated to develop AD, will experience symptoms sooner.

"Even when there already is evidence of amyloid deposition in the brain, if we could find a way to lower tau levels, we would predict that the onset of symptoms may be delayed," says Goate. "But we need to do a lot more cell biology and research in animal models before we can hope to do that."

Aureon Labs, M. D. Anderson Collaborate on Cancer Biomarkers

Six-year-old Aureon Laboratories (Yonkers, N.Y.), which focuses on personalized and predictive pathology testing, has initiated a collaborative research project with the Kleberg Center for Molecular Markers at the University of Texas M. D. Anderson Cancer Center (Houston). With the goal of quantitating and evaluating biomarkers associated with cancer progression and overall survival, the project will use Aureon's systems pathology platform to analyze tissues from approximately 350 non-small cell lung cancer (NSCLC) patients.

According to Vijay Aggarwal, Ph.D., president and CEO of Aureon Laboratories, the company has previously demonstrated the utility of its platform for the stratification of NSCLC patients treated with Iressa and looks forward to further developing its work in this area. Marketed by pharmaceutical companies AstraZeneca and Teva, Iressa (gefitinib) is a selective inhibitor of the epidermal growth factor receptor, which is overexpressed by certain carcinomas.

Aureon's platform applies morphometric imaging to formalin-fixed, paraffin-embedded (FFPE) tissue specimens, enabling quantitation and integration of histological attributes and multiplexed protein biomarkers on a cell-by-cell basis. The company has also developed a multivariate algorithm that integrates histological, molecular, and clinical features to establish a comprehensive "biometric signature" associated with patient outcome. By analyzing the histological and molecular information from tissue specimens, phenotypes associated with disease course can be identified.

The project is expected to complement M.D. Anderson's work to map molecular markers using tissue microarrays. "One of the key features of this study is the ability to use FFPE tissue specimens," noted Ignacio Wistuba, M.D., an associate professor of pathology at M. D. Anderson and principal investigator of the collaborative study with Aureon. "We hope to generate useful information on the biometric signatures associated with NSCLC patient treatment outcome."

ChemoFx Assay Correlates With Improved Ovarian Cancer Survival

Patients with stage II-IV primary epithelial ovarian cancer who received a chemotherapy regimen determined by ChemoFx, a cell-based assay developed and performed by Precision Therapeutics (Pittsburgh), were found to have an overall survival rate 1.4 times longer than those receiving a treatment shown by the assay to be nonresponsive. The study was presented last month at the annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

ChemoFx, which has been covered by Medicare and over 400 commercial insurance companies, assesses the in vitro response of individual patient tumor cells to multi-dose anti-cancer drug exposure. From a small tissue or fluid sample, tumor cells are isolated and maintained in short-term culture before drug testing and their epithelial identity is verified by immunohistochemical staining. The in vitro response of tumor cells to chemotherapeutic agents is then measured by using a range of drug doses. ChemoFx measures the number of live cells remaining

after drug treatment, providing information on both drug-induced cell death as well as inhibition of proliferation.

In the study presented at ASCO, 88 percent of the 206 ovarian cancer patients studied exhibited varying degrees of response to different drugs when evaluated by ChemoFX, despite the fact that all patients had the same type of tumor. The analysis also found that nearly two-thirds of patients' tumors were more responsive to a treatment identified by ChemoFx, than to the treatment they actually received.

Based on these results, researchers used a mathematical model to estimate survival had patients been treated with a drug that ChemoFx identified as more likely to result in a greater tumor response. The analysis found that median overall survival could be extended as much as 23 to 38 months.

"These overall survival data demonstrate that the responsiveness to treatment established by this sensitivity assay in the laboratory setting may in fact translate into meaningful clinical outcomes for patients," said Thomas J. Herzog, M.D., director of gynecologic oncology at the Columbia University Medical Center and lead investigator of the study. "If these results are confirmed in current ongoing trials, this will be a significant step toward establishing individualized treatment strategies for patients who will require chemotherapy."

Panel Advocates Adding HbA1c to Diabetes Diagnostic Criteria

According to the CDC, approximately one-third of people with diabetes do not know they have it, and the average lag between onset and diagnosis is seven years.

In a paper slated to appear in the July issue of the *Journal of Clinical Endocrinology & Metabolism* (*JCEM*), a panel of experts advocates changing the current criteria for screening and diagnosing diabetes. As an alternative to fasting plasma glucose or oral glucose tolerance tests, the panel suggests incorporating another measurement of glucose, hemoglobin A1c (HbA1c), into criteria for screening for and diagnosing the disease.

Approximately 30 percent of people with diabetes in the United States are undiagnosed, according to Christopher Saudek, M.D., of Johns Hopkins School of Medicine (Baltimore, Md.), lead author of the report. "There are serious deficiencies in the current criteria for diagnosing diabetes, and these shortcomings are contributing to avoidable morbidity and mortality."

One reason so many people with diabetes are undiagnosed is because commonly prescribed diagnostic tests—namely the fasting plasma glucose and oral glucose tolerance tests—require that a patient fast for at least eight hours. Because of this requirement, people who have eaten on the day of a doctor visit will not be diagnosed unless they have quite advanced diabetes.

HbA1c testing, which does not require fasting, reflects the average blood glucose level over the previous several months and has long been used to indicate blood sugar levels in patients with diabetes. While widely used by clinicians as a method to assess glycemic control in those established to have diabetes, it has never been officially accepted as a way for doctors to screen for or diagnose the disease.

Current recommendations of the American Diabetes Association were made a decade ago, notes the report, and they rejected the use of HbA1c as a diagnostic tool largely because it was considered at the time to be inadequately standardized and insensitive. Given more recent evidence, the panel believes it is time to revisit using HbA1c and include it as necessary criteria in screening and diagnosing diabetes.

In addition to avoiding the fasting requirement of other tests, HbA1c more accurately reflects longer-term glucose concentration in the blood, while other tests can easily be affected by short-term lifestyle changes, such as a few days of dieting or exercise. And finally, HbA1c laboratory methods are now well standardized and reliable.

The panel recommends that screening standards be established that prompt further testing and closer follow-up. Standards could include HbA1c tests, for example HbA1c greater than 6 percent would qualify as being in need of follow-up; HbA1c greater than or equal to 6.5 percent confirmed by a glucose-dependent test should establish the diagnosis of diabetes.

CDC Report Profiles U.S. Lab Market, Calls for Changes

A new report, commissioned by the Centers for Disease Control and Prevention and released in late May, presents an overview of key factors shaping clinical laboratory medicine throughout the United States, including changes needed in Medicare reimbursement and pathology quality performance. The report, *Laboratory Medicine: A National Status Report* (May 2008), is posted online at *www.futurelab.medicine.org* and is open for comment until June 23. Data from Washington G-2 Reports's Lab Industry Strategic Outlook 2007 is cited throughout the report.

Citing flaws in the current Medicare payment system, the report concludes that the program needs to be redesigned in line with growing scientific, economic, and business challenges in the health care market. The fee schedule method, based on historical charges, is out of date and bears no relation to current production costs or the cost-reducing effects of technological changes, the report says. This is especially true for new molecular diagnostics and other genetic testing. "The processes for establishing reimbursement rates for [them] remain archaic and inadequate."

The report is skeptical that lab competitive bidding will produce substantial Medicare savings and says the current demo model, blocked from a San Diego launch earlier this year after local labs filed suit, is "highly exclusive and could cause significant detriment to labs that lose in the bidding process, since many depend on Medicare for a sizable portion of their revenues."

Redesign of Medicare lab payment would ricochet throughout the national health care system, the report points out. All public payers and approximately 67 percent of private payers use Medicare's payment methodologies as the basis for their own and as tools for negotiating discounts with providers.

The CDC requested the report "to lay the ground work for transforming lab medicine over the next decade." It discusses a range of issues in addition to payment, including workforce shortages, quality performance measures, lab information systems, and federal regulatory oversight. The CDC intends the study to serve "as a reference point for improving quality in the future and as policy guidance for government agencies, professional groups, and others who provide, use, regulate, and pay for lab services."

Report Profiles National Lab Market

- Spending for lab services accounts for 2.3 percent of U.S. health care expenditures and 2 percent of Medicare expenditures.
- Approximately 6.8 billion lab tests are performed annually.
- Lab testing revenues projected for 2007 total $52 billion.
- Clinical pathology comprises 66 percent of all lab tests and $32 billion in revenue.
- Anatomic pathology and cytology account for 23 percent of lab tests and $11 billion in revenue.
- Molecular and esoteric tests account for 8 percent of lab tests and $4 billion in revenue.
- More than 4,000 lab tests are available for clinical use. Of the 1,162 reimbursed by Medicare, about 500 are performed regularly.
- An estimated 1,430 diseases are now detectable using genetic testing. Of these, an estimated 287 are tested only in research settings.
- The number of CLIA-certified labs exceeded 200,000 in 2007. Physician office labs represent 54 percent of the total.
- Hospital-based labs account for 55 percent of total testing volume and 54 percent of total testing revenue, projected at $28.4 billion for 2007.

Source: *Laboratory Medicine: A National Status Report* (May 2008)

The report calls for a number of changes related to pathology. First, it cites a lack of uniformity and standardization of clinical pathology test values among manufacturers that hinders implementation of lab-based guidelines. The report also notes that while laboratory consultations are standard practice and reimbursed for anatomic pathology, this is not always the case in clinical and molecular pathology. The primary barriers to interpretive consultations in clinical pathology are lack of reimbursement and the shortage of subspecialty expertise.

Laboratory Medicine: A National Status Report was prepared by the Lewin Group (Falls Church, Va.) under subcontract to Battelle Memorial Institute (Columbus, Ohio) for CDC's Division of Laboratory Systems (Atlanta) as part of its Improving Quality in Lab Medicine initiative.

Manhattan Physicians Laboratory Buys Genatom Labs

Manhattan Physicians Laboratories, a newly formed independent clinical laboratory led by former Quest Diagnostics executives, has completed the acquisition of Genatom Biomedical Laboratories (Roseland, N.J.). Financial terms of the deal were not disclosed.

From its New Jersey laboratory, Genatom provides predominantly routine laboratory services for clients in the New York-New Jersey metropolitan area and also reaches parts of Pennsylvania and Delaware.

Newly founded Manhattan Labs aims to create "the premier service oriented, high quality independent clinical laboratory in the New York metropolitan area, with a focus on Manhattan." The company is backed by $20+ million in venture capital funding led by Trevi Health Ventures (New York, N.Y.).

"The acquisition of Genatom represents an important first step in Manhattan Labs's strategy," said Manhattan Labs president Thomas Golubic in a statement issued on May 29. "This acquisition will provide us with the initial critical mass and reach to start us on our way to becoming the leading lab in the leading market—Manhattan—in the U.S."

JVHL Partners With Clarient to Expand Test Offerings

The 120 hospital-affiliated labs that comprise the Michigan-based Joint Venture Hospital Laboratories (JVHL; Allen Park) are expanding their anatomic pathology (AP) and molecular diagnostic cancer test offerings through a new partnership with Clarient, the molecular diagnostic and AP specialty lab based in Aliso Viejo, California. Under the current one-year agreement, Clarient will do the technical work at its facility and send results to JVHL pathologists via the Web. The pathologists will then perform the professional interpretation and manage those results with local clinicians.

This partnership will allow JVHL access to expanded AP and molecular diagnostic technology, without having to invest in purchasing the equipment and related infrastructure. "JVHL's desire is to expand their hospital outreach business, and we are giving them the ability to do that without having to go through the additional cost and all that goes with expanding the operations," said David Daly, Clarient's senior vice president of commercial operations. "We're empowering the community pathologists to do what they do best and compete against the larger entities that tend to have a stranglehold on the marketplace." While the partnership is now underway with JVHL's Michigan labs, Daly hopes to expand the arrangement to the system's other labs in Ohio and Indiana.

Genzyme Genetics Plans Expansion in Santa Fe

Tax breaks and other economic incentives from the state of New Mexico are behind the expansion plans of Genzyme Genetics (Cambridge, Mass.). The business unit of Genzyme plans to expand its Santa Fe operations by 45 full-time employees (FTEs) over the next three years. There are over 1,700 FTEs in the entire Genetics division, with 300 currently located at the Santa Fe location.

Through New Mexico's Job Training Incentive Program, Genzyme Genetics will benefit from tax breaks and other economic incentive programs by getting back some of the costs associated with training additional FTEs in lab tech and other support positions, explained Mike Sepata, Genzyme's director of laboratory operations in Santa Fe. Genzyme is accredited by the National Accrediting Agency for Clinical Laboratory Sciences (NAACLS) to train cytogenetic technologists. "The other thing we are leveraging is the state's high wage job credit," he added. "We get a percentage of salary back for every position that is considered high wage. In New Mexico, that cutoff is W-2 earnings of $40,000 or more."

IVD Stocks Gain 4%; Nanosphere Climbs 47%

The 18 stocks in the G-2 Diagnostic Stock Index rose an average of 4 percent in the five weeks ended June 6, with 11 stocks up in price, six down, and one unchanged. The G-2 index is down 10 percent so far this year, while the S&P 500 has fallen 6 percent and the Nasdaq is down 5 percent.

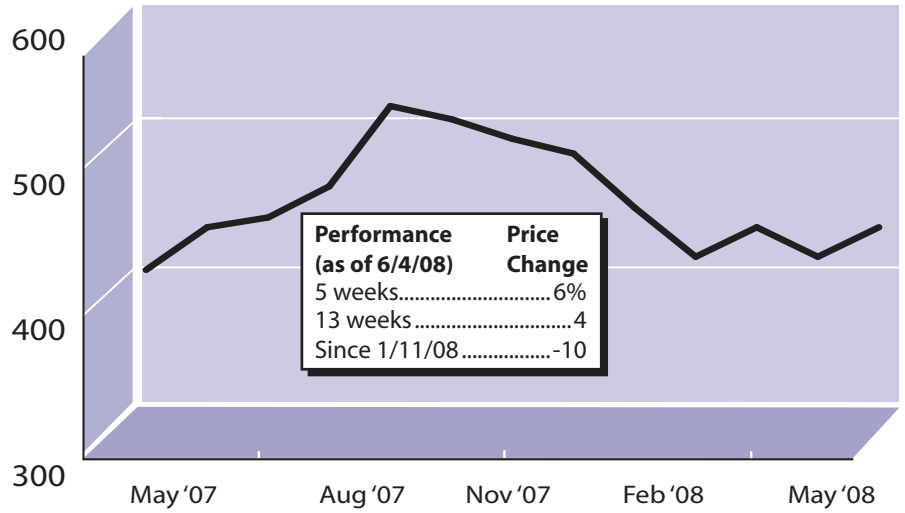
Molecular diagnostics companies have been on the rise in recent weeks. Shares in **Nanosphere** (Northbrook, Ill.) climbed 47 percent to $9.91 a share for a market capitalization of $203 million. The developer and manufacturer of the Verigene system recently announced its first quarter results. First quarter 2008 revenue was $576,000 compared with $270,000 in the first quarter of 2007. "Revenue growth was driven by initial product sales comprised [of] Verigene instruments, reagent rental agreements, and test cartridges," noted CFO Roger Moody on a May 13 conference call with investors.

Nanosphere is now commercializing its ultrasensitive test for cardiac troponin. On the same conference call, CEO and President William Moffitt noted that the company recently initiated "a comprehensive marketing program to begin to position our assay." Next to launch on the Verigene platform will be a cystic fibrosis test, which is now in clinical trials. Added Moffitt, "Additional assays in development scheduled for commercialization over the coming quarters include a respiratory panel, with expectations that we would be in the market by the '08 [or] '09 flu season."

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

Also on the upswing in recent weeks was **Abaxis** (Union City, Calif.). Shares in the company, which manufactures point-of-care blood analysis systems for both the medical and veterinary markets, were up 17 percent to $29.90 a share for a market capitalization of $594 million. The company recently reported record financial results for the fiscal quarter and the fiscal year ended March 31. Quarterly revenues of $26.7 million were up 17 percent over last year's comparable quarter, while revenue of $100.6 million for fiscal 2008 also represented a 17 percent year-over-year increase.

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 18 IVD companies.

Up	Price	% Chg
Abbott Labs	$54.76	3%
Affymetrix	11.92	5
Abaxis	29.90	17
Beckman Coulter	69.95	4
Bio-Rad	86.45	3
Clinical Data	17.32	8
Luminex	21.80	9
Meridian	30.21	8
Nanosphere	9.91	47
Quidel	17.25	5
Third Wave	10.50	17
Unchanged		
Inverness Medical	36.88	0
Down		
Becton Dickinson	82.53	-7
Gen-Probe	52.53	-7
Immucor	26.80	-4
Johnson & Johnson	65.76	-4
Nanogen	0.37	-8
OraSure	5.50	-18

G-2 Insider

Nominate a laboratory leader . . . Washington G-2 Reports is now accepting nominations for its 2008 Laboratory Public Service National Leadership Award, which will be presented at the 26th Annual Lab Institute, "Changing of the Guard: Working With a New Administration, the New Millennial Generation, and a New Health Care System." Lab Institute will take place September 17-19, 2008, at the Crystal Gateway Marriott in Arlington, Virginia.

Presented annually by Washington G-2 Reports, the Laboratory Public Service National Leadership Award honors an individual who has made a significant contribution to the public interest through accomplishments that directly enhance patient care and the laboratory profession. The award recognizes singular accomplishments relative to diverse laboratory industry and professional endeavors in one or more of the following areas: professional advancement; basic or applied research; business creativity and innovations; education and training programs; public policy lifetime achievement; or performance of a special service, task, or project benefiting the laboratory community.

Nominations may be submitted using either an official form available at www.g2reports.com or in a letter that includes the name, title, organization, and contact information of both the nominee and nominator, along with a narrative of 300 words maximum in support of the nomination. Complete nomination forms must be mailed to Washington G-2, 1 Washington Park, Newark, NJ 07102 or faxed to 973-622-6595 no later than July 31, 2008.

References

Abaxis 510-675-6500

ACLA 202-637-9466

Aureon Laboratories 914-377-4000

Clarient 949-425-5700

CMS 877-267-2323

FDA OIVD 240-276-0450

Genzyme 617-252-7500

Hologic 781-999-7300

Innovative Biosensors 301-738-0604

Interleukin Genetics 781-398-0700

JVHL 800-445-4979

Manhattan Physicians Laboratories 866-675-0050

Nanogen 858-587-1121

Nanosphere 847-400-9000

Precision Therapeutics 800-547-6165

Third Wave 888-898-2357

Veridex 585-453-3240

Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by Washington G-2 Reports, 1 Washington Park, Suite 1300, Newark, NJ 07102-3130. Tel: 973-718-4700. Fax: 973-622-0595. Order line: 212-629-3679. Web site: www.g2reports.com.

Stephanie Murg, Managing Editor; Dennis Weissman, Executive Editor; Janice Prescott, Sr. Production Editor; Perry Patterson, Vice President and Publisher; Joe Bremner, President.

Receiving duplicate issues? Have a billing question? Need to have your renewal dates coordinated? We'd be glad to help you. Call customer service at 973-718-4700.