G2 INTELLIGENCE

Diagnostic Testing &Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Vanderbilt to Routinely Test for Genetic Variants Affecting Metabolism of Cardiovascular Drugs

Vanderbilt University Medical Center (Nashville, Tenn.) will begin screening patients who are at high risk for heart disease for a rare genetic variation that can increase the risk of side effects with cholesterol-lowering statin drug simvastatin (Zocor). Initiation of the program is evidence of a growing trend of expanded clinical use of pharmacogenomic testing outside the field of oncology.

The commercially available VeraCode ADME Core Panel (Illumina; San Diego) screens for variants that affect metabolism of other common cardiovascular drugs including clopidogrel (Plavix) and warfarin.

"If you have two copies of the SLC01B1 gene, you're at an almost 20-fold increased risk of muscle toxicity [on simvastatin]," said Dan Roden, M.D., assistant vice chancellor for personalized medicine at Vanderbilt. "We're just reducing the odds. That's what applying genetics at the bedside is all about."

The program kicked off in October in VUMC's adult Primary Care and Cardiology clinics with the goal of enrolling 10,000 patients who may be prescribed common cardiovascular medications. Following testing, the patient's genetic information will be entered into their electronic medical record. For more on the expanded clinical use of pharmacogenomic testing outside of the field of oncology, please see Inside the Diagnostic Industry, page 5.

2011 a Mixed Year for Diagnostics Industry

The year 2011 was a tumultuous one for the diagnostics industry. Some companies were able to thrive with record revenue growth and an increasingly promising pipeline, while others saw revenues plummet and stock prices tumble under the pressure of global economic uncertainties.

"It was a decidedly mixed bag," says analyst Peter McDonald of Auriga USA (New York). "Flat may be a victory this year. It was a tough year. It started off more promising, the summer was tough, but we are [ending the year] cautiously optimistic."

Continued economic pessimism including lingering high unemployment, unresolved federal debt debates, and fears of slashes to federal health spending all took a toll on the industry.

"For 2011 there were a couple of significant overhangs from the investor's point of view on the IVD market. First there were concerns of the macroeconomic

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environment. A subset of that was the trend in declining physician office visits, which led to a decline in lab volumes or slowed growth with correlating impact on diagnostic utilization. The greatest impact was on names most exposed to screening types of tests," says Bill Bonello, managing director, RBC Capital Markets (New York). "The second piece of the macro-overhang was Europe. Bigger players were more impacted, as smaller players are more focused on the United States."

Concerns over cuts to government research grants caused many large research centers to delay investments in large capital purchases and put instrument makers into a downward spiral.

"The tools space was the worst-performing across health care," says Bonello. "In terms of the research tools universe the primary concern was what was going to happen at the National Institutes of Health [NIH]. . . . It is not just about the amount of NIH dollars, but where the dollars are allocated. There had been a big focus on large, de novo genome sequencing projects, now they are more hypothesis-focused [leading to] excess capacity within sequencing."

The pressures on instrument makers were never more pronounced than in the sharp and rapid decline of Illumina (San Diego), whose stock dropped more than 60 percent in the five months since July 2011.

Some Notable Diagnostic Stocks in 2011

(Stock values were calculated over 52 weeks ending Dec. 8, 2011.)

❑ ***Cepheid (Sunnyvale, Calif.) stock up 50 percent.***

For the first nine months of 2011, revenue was up 28 percent to $197.5 million compared to $153.7 million over the same period in 2010. In the company's third quarter of 2011, clinical systems revenue was up 20 percent and clinical reagents revenue was up 37 percent over the previous year.

❑ ***Gen-Probe (San Diego) stock up 11 percent.***

For the first nine months of 2011, revenue was up 4 percent to $407.4 million, compared to $391.6 million over the same period in 2010. In the company's third quarter of 2011, clinical diagnostics product sales grew by 16 percent over the previous year, driven primarily by growth of the APTIMA Combo 2 assay for detecting chlamydia and gonorrhea. This helped to neutralize the 6 percent decline in blood screening sales resulting from lower instrument sales.

❑ ***Genomic Health (Redwood City, Calif.) stock up 40 percent.***

Product revenue for the first nine months of 2011 was $151.6 million, compared with $128.6 million for the first nine months of 2010, an increase of 18 percent.

"The worst-performing [in the tools sector] over 52 weeks was Illumina," says Bonello. "This was a high-multiple, highly valued stock that had been growing and it came to a grinding halt both with growth reported and growth expected."

Analysts say that new product releases helped to overcome some of the macroeconomic forces at play.

"Names with new products performed best over the course of the year," says Bonello. "Cepheid was an outlier stock on the positive side. They had continued excellent placement and growth despite the macroeconomic environment. Genomic Health was a positive outlier in terms of their continued stock performance. Investors are focused on their pipeline and growth opportunities in the future."

Despite a relatively flat stock performance, Myriad Genetics (Salt Lake City) fared well this year, analysts say. Myriad reported large revenue increases in November for its first quarter of fiscal year 2012. The company says its first fiscal quarter revenue increased 20 percent over

the previous year's to $110.5 million. While BRCA testing continued to account for the majority of its molecular diagnostic testing revenue, revenue from the company's COLARIS cancer risk tests, which represents 8.7 percent of total revenue, increased 35 percent to $9.6 million over the same fiscal quarter the prior year.

"Strategic buyers are looking further out than Wall Street."

—Bill Bonello, RBC Capital Markets

"Myriad turned around a bit. Investors are giving their pipeline a little credit, plus BRCA has grown nicely and they are rolling it out in Europe," McDonald tells *DTTR*.

While the outlook for instrument makers may remain sluggish, will IVD manufacturers rebound in 2012?

"I'm cautiously optimistic. We have not recommended many stocks for 2011 and you might say we are getting slightly more bullish as we get closer to 2012," says Bonello. "[We are looking for] stabilization on the utilization front, which would generally be good for these names."

Bonello also expects acquisition activity will continue in the coming year.

"Strategic buyers are looking further out than Wall Street. [When] there is pressure on top-line growth, bigger, slower-growing players look to acquisitions for growth or acquisition synergies to manufacture earnings," says Bonello. "On the target side, who has technology that's attractive? Cepheid, Genomic Health, Gen-Probe is still possible, and Qiagen potentially. These are larger deals, but I would not rule them out. Bigger conglomerates will continue [to acquire]. With Abbott splitting they could be more acquisitive. It wouldn't surprise me to see companies from the outside that have already made a foray [into diagnostics] like GE looking to expand their platform. Large tool companies could be acquirers in the more traditional diagnostic space. I wouldn't rule out an Illumina given the tough few years of growth they are facing."

Universal Cholesterol Screening Recommended for Children

Newly released guidelines say earlier identification of high cholesterol is necessary to substantially reduce the risk for cardiovascular disease (CVD) in young adult life. The guidelines, sponsored by the National Heart, Lung and Blood Institute and endorsed by the American Academy of Pediatrics, strongly recommend a one-time, universal blood cholesterol screening in children aged 9 to 11 years.

Identification of children with dyslipidemias (high blood cholesterol levels) must include a comprehensive assessment of serum lipids and lipoproteins, wrote the expert panel in the guidelines, presented at the annual American Heart Association meeting (Nov. 12-16; Orlando) and published in the December issue of *Pediatrics*.

The expert panel strongly recommends universal screening of cholesterol at least once between the ages of 9 and 11 and again at 17 to 21 with a nonfasting lipid profile (LP). Before age 9 a fasting LP is needed only if there is a family history for early CVD or if the child has any other risk factors including hypertension, diabetes, and a very high body mass index.

"We tried to tie these screenings to adult guidelines which start at around age 20. Basically, we are adding one nonfasting test at approximately age 10," explained Patrick McBride, M.D., professor of cardiovascular medicine, University of Wisconsin School of Medicine (Madison, Wis.), and a member of the panel. "There are a number of barriers. Blood draws in any child are very difficult, fasting, but probably the largest

barrier is physicians' lack of knowledge or agreement with the guidelines."

These recommendations replace previous pediatric guidelines that called for pediatricians to screen high-risk children. The panel cited evidence that a family history of premature CVD or cholesterol disorders as the primary risk-factor in ordering lipid screening in children misses 30 percent to 60 percent of children with elevated cholesterol.

McBride says given the high number of children who are already identified as high-risk and the relatively low price tag per test (an estimated $9 of physicians' costs per in-office test) the recommendations do not represent a large incremental burden. But, he cautions, implementation will be "difficult."

CD4 Most Effective Laboratory Monitoring Strategy for Guiding HIV Therapy in Low-Resource Settings

Quarterly monitoring of CD4 cell counts is the most cost-effective laboratory monitoring strategy for guiding HIV therapy in low-resource settings, according to a new study published in December in the *British Medical Journal*. The study finds that adding CD4 cell counts to clinical monitoring is more effective than clinical monitoring alone or viral load (VL) testing, suggesting a valuable strategy that might allow tight global public health budgets to care for more HIV-infected people.

"Our study suggests not widely implementing a technology (VL testing) that is currently rarely available in resource-poor settings like Africa," says lead author James Kahn, M.D., professor of health policy and epidemiology, University of California San Francisco. "In other words, it's not a question of withdrawing a technology already in place, rather slowing or suspending efforts to widely use VL."

The researchers conducted a randomized clinical trial in Uganda to study cost-effectiveness of quarterly laboratory monitoring options (no lab testing, CD4 testing, or CD4 and VL testing) for HIV patients taking anti-retroviral therapy (ART). The cost of monitoring is driven largely by the cost of the consumable test kit. For CD4 kits are $3.80 of the total $4.68 cost per test and VL kits are $27.20 of the total $29.64 test cost. Adding CD4 cell count to clinical monitoring cost $174 per extra year of health life or disability adjusted life year (DALY), compared to $573 per DALY for putting an additional person on ART in the same setting or $5,158 cost per DALY averted by adding VL to clinical and CD4 monitoring. CD4 monitoring improved clinical outcomes and reduced changes to more expensive, second-line ARTs.

"In addition to being expensive, VL monitoring was not associated with a clinical benefit in addition to CD4 cell count and clinical monitoring," says co-author Jonathan Mermin, M.D., director, division of HIV/AIDS prevention, U.S. Centers for Disease Control and Prevention. "If less-expensive and simpler testing were available, it is likely it would find wider practice in Africa and elsewhere."

According to the authors, routine monitoring of viral load and CD4 cell count during ART was adopted in high-income countries without studies indicating improved survival compared with careful clinical monitoring. By reducing routine laboratory monitoring, there is potential for increasing the number of people who could be treated in resource-constrained environments, if it does not pose a threat to patient morbidity or anti-retroviral resistance.

G2 INTELLIGENCE Inside the Diagnostics Industry

Routine Clinical Adoption of Pharmacogenomic Testing Poised for Gradual Expansion Outside of Oncology

Researchers are optimistic that pharmacogenomic (PGx) testing will make gradual inroads into clinical practice over the next five years, but they say the most notable progress will be in disciplines outside of oncology. Clinical utilization of PGx testing will be propelled by institutional efforts to make health care more cost-effective while improving patient outcomes through personalized medicine.

Oncology is ahead of other medical disciplines in routinely utilizing genetic testing to improve the efficacy of targeted therapeutics, but experts say the field of infectious disease has seen some dramatic changes too, with PGx testing for HIV and Hepatitis C patients becoming the new standard of care.

"The area with a lot of activity in applying pharmacogenomics is in infectious disease, specifically virology," says Howard McLeod, Pharm.D., director, Institute for Pharmacogenomics and Individualized Therapy at University of North Carolina Chapel Hill. "Since [researchers have] found that HIV drugs [are] toxic to a small fraction of the population and that a particular germ line marker can predict who is at risk . . . it is practically malpractice to not use that test."

The U.S. Food and Drug Administration (FDA) recommends and doctors now routinely do pretreatment screenings on HIV-infected patients for the HLA-B*5701 allele, a genetic variant that causes increased risk for hypersensitivity reactions to the anti-viral drug abacavir (Ziagen).

Testing has also permeated disease management for Hepatitis C. While a combination interferon-ribavirin therapy is considered standard of care in treating Hepatitis C, the variability in sustained virological response to the treatment has frustrated disease-management efforts. But the recent incorporation of IL28B genotyping into treatment decisionmaking promises to increase the number of patients for whom treatment is successful while minimizing the number of patients in whom it is deleterious.

Adoption Spreading to Cardiology, Rheumatology, and Neuropsychiatry

Clinical adoption of PGx testing is anticipated to be more gradual in other practice areas, particularly in cardiovascular medicine, where testing for variants in drug metabolism will have to catch up with the brisk dispensation of common prescriptions for statins, anti-aggregants, and blood thinners.

"There are a number of institutions beginning to work on implementation [of PGx programs] most commonly in cardiology and within cardiology using clopidogrel (Plavix) testing," says Julie Johnson, Pharm.D., professor of pharmacy and medicine at the University of Florida (Gainesville).

In 2010 the FDA added a black-box warning to clopidogrel's label to alert physicians about the increased risk for adverse outcomes in patients with mutations in the gene CYP2C19 that lead to poor drug metabolism. In November Transgenomic (Omaha, Neb.) launched the PGxPredict:CLOPIDOGREL Panel, a comprehensive test that analyzes two genes CYP2C19 and ABCB1 and can predict response to clopidogrel in about 50 percent of patients that are poor metabolizers. ABCB1 is covered by a pending patent owned by Transgenomic. The test lists for a price of $750.

"Eight to 10 percent of patients that should be tested are [tested] and that figure could be as low as 5 percent," says Craig Tuttle, CEO, Transgenomic, of utilization of genetic testing to inform clopidogrel dosing decisions. "The challenge is to education physicians."

Genetic testing for the anti-coagulant warfarin is typically cited as an example of the failure of PGx testing to gain routine clinical acceptance, despite evidence showing that it can cut health care spending by reducing costs associated with bleeding events.

"If we look at warfarin there are several barriers. . . . Usually warfarin needs to be started quickly. The delay by ordering the test is undesirable, " explains Johnson. "In academic medical centers warfarin is monitored in specialty anti-coagulation clinics and a lot of clinicians there are comfortable in how they monitor patients. The problem is for patients outside of academic medical centers, where 80 percent to 85 percent of warfarin patients are treated. They stand to benefit the most because they may not be followed as closely. But usually [adoption of new tests] starts in academic settings and moves to the outside."

Non-Oncology PGx Biomarkers with FDA 'Boxed Warnings' or 'Warnings and Precautions'

BIOMARKER	CLINICAL AREA	DRUG
CCR5	Infectious disease - antivirals	Maraviroc
CYP2C19	Cardiology	Clopidogrel
CYP2D6	Psychiatry, analgesics, neurology, urology	Atomoxetine and Iloperidone, Codeine, Dextromethorphan and Quinidine, Tolterodine
HLA-B*5701	Infectious disease-antivirals	Abacavir
HLA-B*1502	Neurology	Carbamazepine
PML/RARα	Dermatology	Tretinoin110

Source: FDA

While cardiovascular medicine's biggest challenge might be altering physician practice, neuropsychiatrists are eagerly anticipating the arrival of PGx tests on the clinical scene.

A study published online Dec. 4 in *Nature Genetics* shows that rare, recurrent copy number variations (CNVs) affecting metabotropic glutamate receptor (GRM) genes were overrepresented in attention deficit/hyperactivity disorder (ADHD) cohorts, appearing in about 10 percent of cases. The current research suggests that selective GRM agonists could be tested as a potential therapy for ADHD in patients harboring particular CNVs. The results could also help in the creation of a diagnostic to assist in identifying which patients would most benefit from the treatment, explains Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics at the Children's Hospital of Philadelphia. Hakonarson explains that a diagnostic may have broader application than just in ADHD given the spectrum of phenotypes including autism and schizophrenia that are affected by mutations in glutamate pathways.

A separate group of researchers made the discovery that dopamine transporter (DAT) and dopamine receptor D4 polymorphisms may be associated with individual variability in methylphenidate dose-response in the therapy used to treat ADHD. Lead author Tanya Froehlich, M.D., says her group's findings, published in October in *Journal of the American Academy of Child and Adolescent Psychiatry*, are "not overwhelming enough that we could [right now] make a clinical test to predict [treatment response] with great certainty," but she says they plan to build a multifactoral model and that further testing using a large, multisite sample is needed.

"It is partly economic," says McLeod of the PGx activity in rheumatology. "The

new drugs are very expensive and only 20 percent of patients get benefit. Insurance companies see it a lousy return on investment. Insurance companies are involved in funding studies looking for a marker. A 50-50 scenario or better would be a more sensible way forward."

Crescendo Bioscience (South San Francisco, Calif.) has released several studies this year supporting its Vectra DA test, a multi-biomarker blood test to assess RA disease activity and treatment response. In the May supplement of *Annals of Rheumatic Disease*, a study showed that following initiation of methotrexate or anti-tumor necrosis factor therapy, RA patients showed changes in their Vectra DA score in as little as two weeks after starting treatment, and individuals' scores were linked to their subsequent clinical response.

"The difference between rheumatology and oncology is that in rheumatology [assessment] is based on clinical impressions—feeling and squeezing joints. . . . Rheumatologist believe there is a better, more quantifiable way to measure disease activity," says David Chernoff, M.D., Crescendo's chief medical officer.

"The new drugs are very expensive and only 20 percent of patients get benefit. Insurance companies see it a lousy return on investment. Insurance companies are involved in funding studies looking for a marker. A 50-50 scenario or better would be a more sensible way forward."

–Howard McLeod, Pharm.D.

In the near future, Chernoff says, he envisions testing to become routine on all newly diagnosed RA patients and in the next three to five years RA may be able to be diagnosed presymptomatically.

Slow, Steady Progress Expected

With increased emphasis on cost-effectiveness and bundled reimbursement, experts say that institutional implementation of PGx programs will likely drive clinical utilization of testing. Greater understanding of the clinical understanding of genetic variations, increased utilization of electronic medical records (EMRs), and improvements in decision support systems will further enhance the value PGx testing.

"Because it is likely that in the not-too-distant future patients will have their full DNA sequence linked to their medical record, it is reasonable to anticipate that all medical specialties will soon be in a position to use this information, especially for genetic variation influencing drug metabolism," says Russell Wilke, M.D., associate professor of medicine in clinical pharmacology at Vanderbilt University Medical Center. "One big obstacle has been limited availability of adequate decision support."

"In the current setting ordering a test adds a delay. Implementation programs are trying to create a model system where the genetic information is available and the lag is avoided," says Johnson. "With preemptive genotyping it changes the question to, 'Can I justify ignoring this information?' The physician community is not opposed to [testing], they just want somebody to make it easier for them."

The experts *DTTR* spoke to unanimously agree that in the next five years there will not be a dramatic increase in utilization of PGx testing. "Once we get to the point that clinicians are at an increased level of comfort interpreting genetic information and have the perception it saves time, there will be increased use. In the meantime we must have dramatic evidence because it takes amazing clinical data or a change in reimbursement," says McLeod.

Court Says Informed Consent Needed for NB Blood Spot Research While Advances in Technology Expand Screening Possibilities

The Minnesota Supreme Court has issued a ruling barring the state from storing and using residual newborn blood spots for research without written informed consent. The decision has implications for the operations of the Minnesota newborn screening program (NBSP) and other such programs nationally.

In overturning the lower courts' rulings, the state Supreme Court wrote in the majority opinion that "the blood samples collected and stored by the Department are 'genetic information' and subject to the restrictions of the Genetic Privacy Act," and because it is genetic information "the Department must have written informed consent to collect, use, store, or disseminate those samples" other than for the screening of newborn children and for follow-up services.

Nine Minnesota families sued the state over privacy concerns. Minnesota has more than 800,000 newborn screening samples in storage. More than 50,000 of the blood samples have been used beyond the initial newborn screening for quality assurance (QA), enhancing newborn screening tests, as well as for research unrelated to the NBSP.

"Saying they must use written informed consent doesn't get into the nitty-gritty of what that means on an operational level. Informed consent is a steppingstone to reassure the public."

—Beth Tarini, M.D.

"This is not the end of the story. There are many more issues to be worked out," says Michelle Lewis, M.D., J.D., research scholar at the Genetics and Public Policy Center, Johns Hopkins University (Washington, D.C.). Those include defining which activities (like QA) fall under NBSP operations and which fall under research. "Where that line is, is unclear. . . . States need to craft policies to protect the operations of NBSP. Limiting the ability to conduct quality assurance activity is potentially harmful."

While the court remanded the case back to the lower court for consideration of remedies, attorneys for plaintiffs in the case said the ruling means the Minnesota Department of Health (MDH) might be forced to destroy stored blood samples. The MDH said it is reviewing the implications of the ruling on operations of the program.

"Saying they must use written informed consent doesn't get into the nitty-gritty of what that means on an operational level," says Beth Tarini, M.D., assistant professor of pediatrics at the University of Michigan. "Informed consent is a steppingstone to reassure the public. . . . The primary issue should be about transparency and an honest dialogue with the public about the value of the spots for the state and the health of the citizens and for research."

Startup to Expand Blood Spot Screening Possibilities

Despite the controversy over use of residual newborn blood spots, advances in testing methods for dried blood spots are expanding screening possibilities. Scientists have developed a rapid mass spectrometry-based method that can be used to simultaneously screen patients for a range of genetic and acquired clinical conditions from a single dried blood spot. The technology, developed by researchers at King's College (London), has

been spun off and launched as SpotOn Clinical Diagnostics (London). The company will initially pursue commercialization of newborn and antenatal screening for haemoglobinopathies and inherited metabolic disorders and the migration of amino acid analysis and acylcarnitines detection into single multiplexed analysis on bloodspots.

"The lessons we have learned from universal presymptomatic screening of newborn babies using dried blood spots can now be cost-effectively applied to provide a personalized medicine approach to the early diagnosis and clinical monitoring of major chronic health problems like diabetes and kidney and heart disease," says Neil Dalton, SpotOn co-founder and a professor at King's College.

Vermillion Buys Correlogic's Assets for IP Buffer in Ovarian Testing Market

In December the U.S. Bankruptcy Court for the District of Maryland approved the sale of Correlogic Systems' (Germantown, Md.) assets to Vermillion (Austin, Texas) for $435,000 in cash. Under the terms of the deal Vermillion will acquire diagnostic samples, software, and intellectual property (IP) related to Correlogic's ovarian cancer diagnostics business.

In a November conference call to discuss third-quarter financial results, Vermillion CEO Gail Page called the purchase strategic, saying it could save sample collection time as well as offer further "IP protection." The deal was announced following the settlement of Correlogic's dispute with Quest Diagnostics (Madison, N.J.) and Laboratory Corporation of America (Burlington, N.C.) regarding rights to OvaCheck test. Correlogic filed for Chapter 11 bankruptcy on July 16, 2010, and in March 2011 attempted to auction its assets, but efforts were hampered because of the ongoing dispute.

Correlogic claimed its 2002 OvaCheck licensing agreements with Quest and LabCorp were invalid because they did not cover the transition of the test from mass spectrometry to an immunoassay-based test. According to reports, under the terms of the November settlement the parties agreed that Correlogic will provide a nonexclusive license to Quest and LabCorp to all IP rights to the OvaCheck test as it existed prior to the company's bankruptcy filing in exchange for a cash payment of $75,000. The agreement expressly excludes IP to the second-generation OvaCheck diagnostic that Correlogic has been working on since its bankruptcy filing. Vermillion will receive the rights to the newer OvaCheck2, but according to Page, Vermillion does not plan to commercialize the test.

Concateno Launches Roadside Drug Test; Tests for Five Drugs in Five Minutes

Concateno (Oxford, England), a subsidiary of Alere (Waltham, Mass.), is launching a next-generation roadside drug testing device capable of detecting if a driver is under the influence of up to five drugs from a single oral fluid sample within five minutes.

The company unveiled the CE-marked Alere DDS2 Mobile Test System at Medica 2011 (Dusseldorf, Germany) in November. The handheld device enables police to determine if a driver is under the influence of cocaine, cannabis, opiates, amphetamines,

or methamphetamines. Future testing panels will include buprenorphine, ketamine, and methadone, the company says. The system improves upon its previous Cozart DDS system with advances including greater cannabis sensitivity, a wider temperature range, and a color screen for better viewing under roadside conditions. The device can also store up to 10,000 results using the accompanying Data Manager Software, which also measures positivity rates and generates drug trend reports.

Concateno is considering commercializing the product in the United States given police interest. A company spokesperson says the device can be used in a workplace context, "particularly where a guideline indication of illicit drug use is required on-site, for example in health and safety-critical posts" or in post-incident testing. The test cost depends on volume and the range of drugs tested, but each test could cost from about £10 ($15), the company says.

Pathwork Molecular Tissue of Origin Test Changes Pathologists' Final Opinion More Than Half the Time

Pathwork Diagnostic (Redwood City, Calif.) continues to build the case for the effectiveness of integrating its Tissue of Origin (TOO) test into clinical practice for cases of metastatic cancer. Their latest findings, presented in November at the Association for Molecular Pathology annual meeting, show that in more than half of cases pathologists changed their initial or unresolved differential diagnosis based on the results of the gene expression profiling test.

Researchers presented findings from a retrospective study of cases referred for TOO that had difficult-to-diagnose carcinomas with three or more possible sites of origin. In six of the 23 cases the test concurred with the original diagnostic interpretation and in two cases the test results were below 20, the lowest meaningful score. But in 13 out of the 15 cases that the TOO test indicated a site of origin different from the initial pathologist-favored site, the pathologist changed their final opinion in favor of the TOO result. In two of those cases a clinically assumed primary lesion proved to be metastatic.

The microarray test measures the expression of more than 2,000 genes in a tumor and compares it to expression patterns of a panel of 15 known tumor types, covering 90 percent of all solid tumors. The test, which was cleared by the U.S. Food and Drug Administration in 2010, is covered by Medicare and is offered for $4,000 to $5,000—a price David Craford, Pathwork's chief commercial officer, says is worthwhile given the need to correctly identify tumor origin to achieve benefit from new, expensive, targeted therapies and given that patients with difficult-to-diagnose primary cancers can undergo 10 or more immunohistochemistry tests.

"There is a need [for the test], for a subset of patients whose tumor origins can't be identified," says lead author Maressa Pollen, M.D., a molecular genetics pathology fellow at Vanderbilt University. "Pathologists, like all people, fall into two camps—early adopters and people who need more information. If there is enough evidence, then they will feel confident in trusting the new technology. . . . But [the TOO test] has its place and is beneficial and the study shows that."

G2 Index Drops 5%, Despite Acquisitions

The G2 Diagnostic Stock Index was down 5 percent for the four weeks ending Dec. 16. For the four-week period, four stocks rose modestly, while 13 stocks declined. The Nasdaq and the S&P also declined over the same period, with the Nasdaq losing 5 percent and the S&P losing 3 percent.

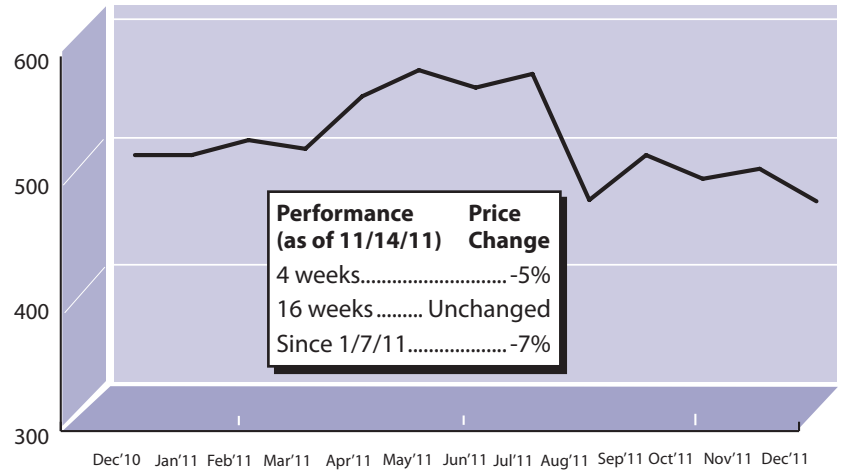
The G2 Diagnostic Index closed 2011 dropping more than 7 percent, slightly more than the Nasdaq and S&P, which lost 5 percent and 4 percent for the year, respectively. Ten stocks lost ground in 2011, while seven gained in value. Among the biggest losers for the year were San Diego-based Illumina and Sequenom, which both declined more than 50 percent over the year. OraSure (Bethlehem, Pa.) and Cepheid (Sunnyvale, Calif.) were the companies whose stocks grew the most, 44 percent and 34 percent, respectively.

Despite news of acquisitions Affymetrix (Santa Clara, Calif.) and Alere (Waltham, Mass.) were not able to overcome the market's downward pull in the last four-week period. Affymetrix, whose stock declined 22 percent for the period, had previously announced that it would acquire eBioscience Inc. (San Diego) for $330 million financed by cash on hand and committed debt. The transaction is expected to close late in the fourth quarter. In a statement Affymetrix CEO Frank Witney, Ph.D., said the acquisition was expected to be "transformational" in helping the company diversify its revenue and molecular diagnostics business by gaining flow cytometry and immunoassay reagents used in immunology and oncology.

"This transaction places Affymetrix at the forefront of immunology and oncology, two of the fastest-growing segments of molecular and translational medicine," said Stephen Fodor, Ph.D., founder and chairman of Affymetrix.

Alere's shares dropped 12 percent for the four-week period. In a move expected to boost growth, Alere acquired Arriva Medical (Coral Springs, Fla.), a provider of diabetes testing supplies to individuals in their homes. Arriva had sales of $21.5 million for the half year ending Oct. 31, 2011. Alere paid about $65 million in cash and 806,452 restricted shares of its common stock.

G2 Diagnostic Stock Index



Source: The G2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 19 IVD companies.

Up	Price	% Chg
Abbott Labs	54.89	1%
Abaxis	27.74	3
Luminex	20.71	1
OraSure	9.06	3
Down		
Affymetrix	3.80	-22%
Alere	22.87	-12
Becton Dickinson	70.65	-5
Bio-Rad	97.07	-4
Cepheid	31.40	-9
Gen-Probe	56.50	-9
Illumina	26.91	-15
IRIS	8.96	-3
Johnson & Johnson	64.30	-1
Meridian	18.30	-1
Qiagen	13.52	-7
Quidel	15.90	-9
Sequenom	3.73	-10

G2 Insider

MDx and ID Tests Most Likely to Be Added to Lab Menus, G2 Survey Found ...
Two-thirds of clinical laboratories responding to a diagnostic testing survey conducted by G2 Intelligence say they are currently offering molecular diagnostic testing (MDx) or are considering adding molecular tests to their menu.

Of the 51 labs responding to an e-mail survey conducted in October, 42 percent said they currently offer MDx and plan to expand their molecular offerings and 24 percent said they are considering adding some molecular tests to their menu, while 32 percent said they cannot financially justify offering MDx.

Almost all respondents said that changes to the test menu are driven by physician demand, revenue potential, and the desire to reduce send-out costs. When asked what type of tests they are most likely to add in the near future, 68 percent said infectious disease testing, followed by oncology (36 percent), cardiovascular testing (30 percent), and genetic testing for inherited disorders (24 percent).

When asked about advances in point-of-care testing, 52 percent of respondents said it would help them by reducing turnaround times, while 38 percent said it would hurt them by reducing test volumes.

The most significant challenge responding labs face is reimbursement concerns, followed by personnel shortages, competition from national labs, regulatory uncertainties for lab-developed tests, competition from local labs, and consolidation of laboratories. Also mentioned was the challenge of reinventing the lab for the era of accountable care organizations.

Of the 51 labs responding to the survey, 32 (63 percent) were hospital/health systems labs, 9 (18 percent) were physician office labs, one was a private pathology practice, three were independent labs, and six fell into the "other" category (academic medical center, dialysis lab).

Company References

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