Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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CONTENTS

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Gen-Probe Acquisition Typifies M&A Trends

Closing what was a good year for mergers and acquisitions in the laboratory and diagnostics space, Gen-Probe Inc. (San Diego) acquired GTI Diagnostics (Waukesha, Wis.) at the end of December. Gen-Probe paid $53 million in cash for the privately held diagnostics company focused on coagulation and transfusion-related blood bank products.

The acquisition is a strategic play for Gen-Probe, boosting its transplant diagnostics business acquired from Tepnel Life Sciences in 2009 and providing entry into the blood-banking and coagulation markets.

GTI develops and manufactures the human leukocyte antigen (HLA) antibody screening products sold by Gen-Probe under its Lifecodes brand. GTI also commercializes a number of other HLA-related testing products, including a range of molecular typing products for donor-recipient matching and patient monitoring, as well as immunoassay products for the coagulation and blood bank markets.

This acquisition typifies what experts see as a growing trend of deploying recently burgeoning cash on hand for strategic acquisitions. For more on expected trends in mergers and acquisitions, see *Inside the Diagnostics Industry, p. 5.*

MGH and Johnson & Johnson to Collaborate on CTC Technology

Oncology diagnostic company Veridex LLC (Warren, N.J.) and Boston-based Massachusetts General Hospital (MGH) have announced a partnership to develop and commercialize next-generation circulating tumor cell (CTC) technology for capturing, counting, and characterizing tumor cells. The collaboratively developed bench-top system will use CTCs both as a diagnostic tool for personalizing patient care and to accelerate targeted drug development.

The MGH team already developed a microfluidic chip capable of capturing a single tumor cell among billions of healthy cells. However, in an attempt to push the limits of early detection, Mehmet Toner, Ph.D., a developer of the chip and director of the MGH BioMicroElectroMechanical Systems (BioMEMS) Resource Center, says the new technology being developed in the partnership, while based on similar fundamental principles, will aim for even higher sensitivity and lower production costs, encouraging eventual mass production and widespread utilization. The current chip costs "less than $200" to produce.

Continued on p. 2

▲ **MGH and Johnson & Johnson to Collaborate,** *from page 1*

"We anticipate the next generation will not use a solid surface," says Bob McCormack, head of technology innovation and strategy for Veridex, a Johnson & Johnson company. "The most important difference is the next-generation technology is going to be fully automated for both numeration and characterization. It is going to be a system that a laboratorian can walk over to a computer and program in all of the questions, and the technology will do the rest.

"Currently, we are between concept and prototype," assesses McCormack. "There is a lot more in front of us to do, but we hope to get there quickly." Some have estimated five years until the new technology is available.

MGH's CTC chip contains 78,000 microscopic columns, each with an antibody coating capable of attaching to circulating tumor cells and trapping the cancer cell intact. Using a $15 million grant from Stand Up to Cancer, MGH, Sloan-Kettering (N.Y.), University of Texas M. D. Anderson Cancer Center, and Dana-Farber Cancer Institute (Boston) will start clinical tests of the chip in the next few months.

The chip, described as a "liquid biopsy," could make it possible to analyze cancers of the internal organs in real time, noninvasively, from diagnosis, detecting, and characterizing cancers to treatment, targeting therapies, and monitoring drug effectiveness.

Aside from the presumed clinically actionable applications of CTC technology, the chip holds potential for researchers. "Much of the basic science research is conducted in animal models, but with this we can learn about the cells, develop new drugs, identify biomarkers, and learn the basic science of cancer in real cells," adds Toner.

Veridex will assist in the clinical validation and regulatory submissions for the new technology based on their experience bringing CellSearch, their Food and Drug Administration-cleared CTC technology, to market in 2004. The collaboration also involves another Johnson & Johnson unit, Ortho Biotech Oncology Research & Development.

Gestational Diabetes Screening Rates Too Low

As experts debate adopting new stricter, international recommendations for gestational diabetes mellitus (GDM) screening, a new study shows screening rates in the United States are lower than current guidelines set by the American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA).

In the study, published in the January issue of *Obstetrics and Gynecology*, researchers from Quest Diagnostics (Madison, N.J.) found that 32 percent of pregnant women are not being screened for GDM. Of the nearly 633,000 pregnant women who were tested, 4.9 percent tested positive for GDM under existing criteria. If the guidelines recommended by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) were used, the researchers found the number of GDM-positive women would have doubled using the 75 gram oral glucose tolerance test (OGTT).

The IADPSG recommendations replace the 100 gram OGTT with the 75 gram OGTT and lower the glucose threshold values for the fasting and two-hour measures. In the Quest study, 90 percent of the 166,000 confirmatory tests were done using 100 gram OGTT demonstrating that significant adjustment in clinical practice would be necessary to adopt the new, international recommendations.

The study also found that only one in five women with GDM was screened for diabetes postpartum despite ACOG and ADA guidelines stating all women with GDM should be screened for diabetes six to 12 weeks postpartum.

23andMe to Validate Web-Based PGx Research

23andMe Inc. (Mountain View, Calif.) will use a grant from the National Institutes of Health to launch a project to validate a Web-based platform for pharmacogenomics research.

The project will try to replicate known genetic factors influencing the efficacy and tolerability of three classes of medications—the blood thinner Warfarin, proton pump inhibitors prescribed for acid reflux, and nonsteroidal anti-inflammatory drugs (NSAIDs)—using Web-based survey data. Initially the team will validate the use of Web-based surveys to assess the drug side effects and drug effectiveness experienced directly by the company's customers. Subsequently, the researchers aim to replicate previously known associations between response to the drugs and variation within two genes: CYP2C9 and CYP2C19.

In previous studies, 23andMe has demonstrated that self-reported information from customers yields data of comparable quality to that gathered using traditional research methods. The company says that validation of a large-scale, cost-effective, and rapid approach for discovering new pharmacogenomic markers would be a significant contribution to personalized medicine.

The Web-based surveys have been drafted and are currently under review by a panel of pharmacogenomics experts.

"23andMe believes that Web-based research has the ability to accelerate genetic research at an exponential rate," Joanna Mountain, Ph.D., senior director of research at 23andMe, tells *DTTR*. "Removing the barriers of time and geography to research enables larger numbers of people to participate in research, and sheer numbers make it more likely that novel genetic associations will be identified and that findings will be statistically significant."

In January the company also announced the addition of $9 million to the $22 million of Series C Financing announced in November. MPM Capital and Johnson & Johnson Development Corp. are new C-round investors. The capital raised in this round will be used to accelerate research.

New Studies to Improve Accuracy of PSA Testing

Despite its high rate of false positives, the prostate-specific antigen (PSA) remains the most widely used marker for prostate cancer screening. Two recent studies highlight research into how to make the PSA screening test results more meaningful both in men on 5-alpha reductase inhibitor (5ARIs) for enlarged prostates, as well as the overall male population with a method for personalizing PSA cutoff values.

Any PSA Increase While on Dutasteride of 'Grave Concern'

The Reduction by Dutasteride of Prostate Cancer Events (REDUCE) study demonstrates that while the initial decrease in PSA from dutasteride (Avodart) does not predict the likelihood of prostate cancer, any subsequent rise in PSA while on the drug indicates an increased risk for high-grade, clinically relevant tumors.

The study, published in the January issue of the *Journal of Urology*, involved 8,200 men

ages 50 to 75 with elevated PSA levels (2.5 ng/ml to 10 ng/ml), but negative biopsies. Men taking dutasteride were twice as likely to have aggressive prostate cancer if their PSA levels rose, compared to men whose PSA levels went up while taking a placebo. In men with any magnitude of increase in PSA, aggressive, high-grade tumors were diagnosed in 13.2 percent of those on dutasteride and in 7.7 percent of those taking a placebo.

"Any confirmed PSA rise, of any magnitude, from nadir is a strong signal that a detailed evaluation is necessary. Any rise off of baseline is of grave concern," says Gerald Adriole, M.D., chief of urologic surgery, Washington University School of Medicine in St. Louis. "Doctors can be confident they are not missing any other cancers. PSA is not a perfect test, but the miss rate is lower [if you look at the confirmed rise in PSA]."

While the authors do not recommend taking dutasteride other than for treatment of an enlarged prostate, they conclude that dutasteride treatment enhances the usefulness of PSA by reducing the diagnosis of low-grade cancers that are unlikely to cause harm if untreated and elucidating aggressive cancers not responding to dutasteride therapy.

GlaxoSmithKline, the manufacturer of Avodart, sponsored the study.

SNPs Can Personalize PSA Biopsy Threshold

Identification of six single nucleotide polymorphisms (SNPs) that impact both individual baseline levels of PSA and risk of prostate cancer has the potential to personalize PSA thresholds, more accurately identifying those men at risk for a positive biopsy, according to a study published online in December and appearing in a future print edition of *Science Translational Medicine*.

Researchers note that inherited factors account for 40 percent of variability of PSA levels in the general population. This variability often hampers effective utilization of results from the PSA screening test with roughly 40 percent of men with PSA levels greater than 10 ng/ml having no evidence of prostate cancer at biopsy.

The international team of researchers, led by Decode Genetics, used genomewide association analysis of 15,800 Icelandic men and validated the results in a U.K. cohort. The researchers subsequently analyzed 47,000 men with prostate cancer and matched controls from five countries to determine that two of the SNPs (10q26 and 12q24) are linked exclusively to PSA levels, while four additional loci are associated with both PSA levels and prostate cancer risk.

The authors conclude the new markers primarily predict the outcome of PSA-based prostate cancer screening. By applying a "genetic correction" to commonly used PSA cutoff values, almost 7 percent of Icelandic men had at least one PSA measurement shifted above or below the biopsy cutoff and were reclassified.

"The challenge is to more effectively risk stratify the population, identifying and biopsying those at high-risk and with aggressive disease while minimizing the number of negative biopsies we perform," said study author Kari Stefansson, M.D., CEO of Decode Genetics, in a statement. "The SNPs reported today enable us to personalize PSA thresholds, thereby changing the recommendation on whether to biopsy for a substantial proportion of men."

Stefansson added that Decode is working "to swiftly incorporate" these PSA markers into the company's testing portfolio.

M&A Set to Increase in 2011, Driven by Strategic Product Targets

Mergers and acquisitions (M&A) continued to rebound in 2010 throughout the diagnostics and lab industry, with experts predicting both increased activity and rising valuations in 2011. Driven by large amounts of cash on-hand and the desire to find strategic acquisition targets to fill out product lines and expand geographic market presence, buyers will likely be conservative, searching for differentiating products that are producing revenue or close to commercialization.

"I definitely think M&A is more strategic," says Jeff Frelick, senior analyst, diagnostics and life science tools, Conaccord Genuity, a global investment bank with offices in the United States, United Kingdom, Asia, and Canada. "Valuations in 2009-2010 were fairly attractive after being beaten up. Now we are getting strategic buyers looking for attractive assets where they have voids to fill in their pipeline."

Strategic acquisitions in 2010 could be classified as serving two primary purposes—either fortifying an existing market presence through acquisition of complementary technology or as purchasing a presence in either a new geographical market or product area.

Strategic Acquisitions

2010 acquisitions that fortified an existing market presence:

- In late December **Transgenomic** (Omaha, Neb.) completed the acquisition of the diagnostic business of **Clinical Data Inc.** (Newton, Mass.) for $15.5 million. The acquisition strengthened the marketplace molecular diagnostics offerings with an established revenue base and expanded commercial operations with an additional CLIA-certified lab.
- **Laboratory Corporation of America's** (LabCorp) $925 million cash bid for **Genzyme Genetics** was finalized in December. The buy strengthens LabCorp's position as a provider of personalized medicine products for cancer.
- Swiss drugmaker **Roche Holding AG** bought **BioImagene** (Sunnyvale, Calif.), maker of digital pathology products, for approximately $100 million in August, to further its position in tissue-based cancer diagnostics. BioImagene brings to **Ventana Medical Systems Inc**., a member of the Roche Group, added capabilities for scanning and analyzing tissue by creating high-resolution, whole-slide digital images from glass microscope slides.
- In May **Thermo Fisher Scientific** (Waltham, Mass.) acquired **Fermentas** (Ontario, Canada), a manufacturer and distributor of enzymes, reagents, and kits for molecular and cellular biology research for $260 million in cash. Thermos Fisher said the acquisition will strengthen its capabilities in the high-growth polymerase chain reaction (PCR) market, including research and PCR-based testing.

2010 acquisitions that allowed entry into a new product or geographic market:

- In December **GE Healthcare** closed its $580 million acquisition of **Clairent** (Aliso Viejo, Calif.), an anatomic pathology and molecular testing services company. The purchase greatly enhances GE's presence in clinical lab services and personalized medicine, specifically in cancer diagnostics, and is one in what many believe will be a continued series of expansions of GE's presence in the molecular diagnostics space, as witnessed by its May $5 million investment in **CardioDx** (Palo Alto, Calif.), a maker of noninvasive cardiac genomic tests.
- **Sekisui Medical Co. Ltd**. acquired **Genzyme's Diagnostic** products business for $265 million in cash. Sekisui Medical is based in Tokyo and sought to expand its global presence.

The slowly improving economy helped stimulate M&A activity in 2010. After several years of holding on to cash, companies were looking for to put their cash-laden balance sheets to work, say experts. The debt-to-equity ratios were low throughout the industry and, with signs of a strengthening economy, some companies were willing to take on credit.

"There is no shortage of capital interested in lab industry deals now, while there was, in the real depths of the economic crisis," Chris Jahnle, co-founder and managing director at Haverford Healthcare Advisors (Paoli, Pa.), tells *DTTR*. "There was a real decline in acquisitions in part due to debt capital markets being frozen, but it is thawing now. Valuations have recovered, maybe not to 2007-2008 levels, which were the highest acquisition prices we have seen, but valuations will climb throughout 2011."

Jahnle says he sees consolidation as a key trend affecting the outlook for M&A activity in the laboratory space in the upcoming year and he looks to two active 2010 acquirers to keep up the pace. Pathology laboratory Aurora Diagnostics (Palm Beach Gardens, Fla.) completed five acquisitions in 2010, with two closing in December, says Jahnle, who exclusively represents Aurora on the buy-side.

"Aurora continues to pursue acquisitions of small laboratory companies," he notes. "The industry remains fragmented with thousands of independent pathology practices and laboratories, and Aurora raised $200 million of debt effective Dec. 14, 2010, and has a lot of capital to continue to pursue acquisitions into 2011."

Aurora is not the only active laboratory buyer. In November Sonic Healthcare of Australia announced a $123.5 million acquisition of CBL Pathology (Rye Brook, N.Y.), a specialty lab offering anatomic, molecular, and digital pathology services.

"Historically, Sonic has peacefully coexisted with pathologists and focused on providers—clinical laboratories servicing physicians' offices. So this was a marked, dramatic departure from historical behavior," comments Jahnle. "It looks to be an acquisition-oriented company and the parent company has made tremendous investments in anatomical and pathology labs in EU and Australia, so why should the U.S. be different?"

Another driver of laboratory acquisitions were the Bush tax cuts.

"A lot of transactions were done because sellers wanted to sell before capital gains tax rates were scheduled to increase, with a flurry of activity at the end of the year," explains Jahnle. "Now that they have been extended for two years, some who have been on the fence about selling will want to get in line before the potential risk of capital gains tax increases. This will increase small-deal activity; it won't affect a [company like] Genzyme."

As small deals are predicted to abound in the laboratory space, the molecular diagnostics industry is poised for some large transactions in 2011.

Thermo Fisher Scientific's (Waltham, Mass.) $2.1 billion acquisition of Dionex (Sunnyvale, Calif.) is set to close in first quarter of 2011. Thermo Fisher intends to

use cash on hand and proceeds from committed financing from Barclays Capital and J.P. Morgan Securities LLC to facilitate the transaction. Dionex will expand ThermoFisher's presence in chromatography to include ion and liquid systems and provides an expansion opportunity into Asia-Pacific markets.

Also heating up the acquisitions outlook is the fact that Beckman Coulter (Brea, Calif.) and Genoptix (Carlsbad, Calif.) are both shopping for buyers. The *Wall Street Journal* reported in December that Beckman, which had 2009 revenues of $3.3 billion and an approximate market capitalization of $5 billion, retained Goldman Sachs to help with its strategic options, including a possible sale of the company to private equity firms. Genoptix (Carlsbad, Calif.), a laboratory services company specializing in cancer diagnostics, hired British investment bank Barclays to begin an auction process, *Bloomberg News* reported. The company had $184 million revenue in 2009 and a $316 million market capitalization.

Sampling of 2010 M&A Deals

ACQUIRER	SELLER	PRICE (in U.S. $)	REVENUE MULTIPLE	MULTIPLE	VALUE TO ACQUIRER
LabCorp	Genzyme Genetics	$925 M	$371 M	2.49	Strengthens offerings in oncological personalized medicine
GE Healthcare	Clarient	$580 M	$91.6 M	6.33	Expands into cancer diagnostics services
Sekisui Medical Co.	Genzyme Diagnostics	$265 M	$167 M	1.59	Expands global presence
Thermo Fisher Scientific	Fermentas	$260 M	$54 M	4.81	Strengthens its capabilities in the high-growth PCR market
Roche Holding AG	BioImagene	$100 M	--	--	Provides added capabilities for scanning and analyzing tissue
Quidel	Diagnostics Hybrid	$130 M	$51 M	2.55	Expands continuum of diagnostics testing products across patient care
Gen-Probe	GTI Diagnostics	$53 M	--	--	Boosts its transplant diagnostics business
Transgenomic	Clinical Data	$15.5 M	$9.9 M (PGx-Health test revenue)	1.52	Strengthens molecular diagnostics offerings and expands operations

Source: Washington G-2 Reports

Other big industry players will likely get in the action this year.

"Gen-Probe is constantly looking," speculates Frelick. "They probably have several targets in their sights. What will they pull the trigger on is the question."

While reimbursement, regulatory, and political uncertainties are always looming, most see 2011 as a promising year.

"Executives in the laboratory industry are just about immune to politics and regulatory change. They have been battered around with threats of reimbursement compression and utilization compression for so many years now," says Jahnle. "Lab testing is a great health care spend and early detection is a great investment. An aging population trumps political headwinds."

Court Upholds Methods Patents; Infringement Suits Dismissed

Federal courts recently issued rulings in two intellectual property cases, one of which could impact patent standings throughout the molecular diagnostics industry.

In December, a U.S. district court dismissed two patent-infringement suits Illumina (San Diego) filed against Affymetrix (Santa Clara, Calif.) in May 2009. The U.S. District Court for the Western District of Wisconsin granted a summary judgment of noninfringement for Affymetrix on Dec. 15.

The suit asserted that a variety of array plate products and a related scanner (GeneChip and GeneTitan) by Affymetrix infringed on the "841" patent Illumina was awarded in March 2009. The patent (U.S. Patent No. 7,510,841) is titled, "Methods of Making and Using Composite Arrays for the Detection of a Plurality of Target Analytes."

"Because the undisputed facts show that the accused products do not include a 'substrate,' as required by each of the asserted claims, I will grant summary judgment to defendant," wrote District Judge Barbara Crabb in her decision.

Prometheus Case

In a much more anticipated ruling, the Court of Appeals for the Federal Circuit in Washington handed down a ruling nearly identical to its 2009 decision upholding methods patents on diagnostic tests owned by San Diego-based pharmacogenomic test manufacturer Prometheus.

As in its previous ruling, the appeals court stated that Prometheus's patents satisfy the "machine or transformation" (MOT) test for patentable subject matter. The Prometheus patents involve initial dosing of thiopurine drugs (used for treating autoimmune disorders), measuring metabolites of the drug in the blood, and determining the patient's optimal dose.

The *Prometheus v. Mayo* case was appealed to the U.S. Supreme Court but was remanded back to the Federal Circuit for reconsideration in light of decision in *Bilski et al. v. Kappos*, a patent case in which the Supreme Court ruled that the MOT test may be useful but should not be considered the sole test for determining patent eligibility of methods. This is the first diagnostics case to be considered by the Federal Circuit since the *Bilski* decision.

Legal experts say that the Federal Circuit appears reluctant to narrow the scope of patentable subject matter. This is the same court that will hear the appeal in the Myriad gene patent case, in which a lower court invalidated some of the Utah-based company's gene and methods patents related to the BRCA test for breast and ovarian cancer gene mutations.

While it is uncertain when the Federal Circuit will decide the Myriad case, "it's hardly a stretch to think that Myriad remains headed for at least a partial reversal," posts Dan Vorhaus, a lawyer with Robinson Bradshaw & Hinson, P.A. and editor of the firm's *Genomics Law Report*. Vorhaus speculates that lower court Judge Sweet's findings that Myriad's diagnostic claims for analyzing genetic sequences failed to satisfy the Section 101 test for patentable subject matter are particularly at risk for a reversal.

Breast Cancer Studies Highlight Impact of Molecular Testing

Several studies presented at the 33rd annual Cancer Therapy and Research Center (CTRC)-American Association for Cancer Research (AACR) San Antonio Breast Cancer Symposium, held Dec. 8-12, 2010, highlighted the impact molecular testing can have on predicting cancer reoccurrence and metastatic progression.

CTCs Predict Metastasis in Breast Cancer Patients

Researchers from the University of Texas M. D. Anderson Cancer Center retrospectively evaluated a cohort of 408 women with metastatic breast cancer (MBC) and confirmed radiological progression of disease. The rate of development of new metastatic sites was compared according to baseline values of circulating tumor cells (CTCs). New metastatic sites developed in 22 percent of patients with CTC values less than five and in 32 percent of patients with CTC greater than five. Patients presenting with baseline CTC values of five or more and with bone metastases without visceral involvement had the highest rate of development of new metastatic sites.

The researchers concluded that since a high, baseline number of CTCs most significantly predicted new metastatic sites in patients with initial bone involvement, bone-directed therapies for MBC patients with CTCs of five or more should be evaluated.

Ki67 Proliferation Index to Identify Early Nonresponders to Endocrine Therapy

Ki67, a protein marker for tumor proliferation, is factored into the prognostic tool PEPI (Preoperative Endocrine Prognostic Index). One of the constraints of PEPI is that it takes four months of treatment to identify estrogen-receptor-positive (ER+) breast cancers that have a poor long-term outcome. By assessing tumor response to endocrine therapy sooner, nonresponding tumors can be triaged to neoadjuvant chemotherapy.

Early Ki67 assessment does identify patients with poor outcome ER+ disease, and Ki67 measurement of more than 10 percent accurately predicts higher rates of relapse.

Researchers at Washington University School of Medicine in St. Louis evaluated the utility of an assessment of the Ki67 level in a tumor biopsy sample taken two to four weeks after initiating treatment in neoadjuvant endocrine therapy trials for early identification of nonresponders. In the study Ki67 levels were measured in 158 post-menopausal women with confirmed ER+ stage II and III breast cancers two to four weeks into endocrine therapy.

They found that early Ki67 assessment does identify patients with poor outcome ER+ disease and that Ki67 measurement of more than 10 percent accurately predicts higher rates of relapse. High-quality tumor samples obtained from patients in the study will be used for molecular profiling and will help investigators determine the molecular basis for endocrine therapy resistance.

Breast Cancer Index Predicts Recurrence

Data presented by BioTheranostics (San Diego), a bioMerieux company, show that the company's Breast Cancer Index (BCI) molecular test can quantitatively assess the risk of distant disease recurrence. The data also demonstrated that HOXB13, a protein-

coding gene part of the Breast Cancer Index, predicted patient benefit from letrozole among ER+ breast cancer patients.

Researchers from Massachusetts General Hospital retrospectively evaluated the ability of the BCI to distinguish those patients at risk of late recurrence and those who would respond to extended therapy with letrozole. The patients had participated in the MA.17 study to determine whether letrozole improves outcome after discontinuation of tamoxifen.

"It is our understanding that this is the first time a biomarker has been validated exclusively in the 'late recurrence' setting," said study investigator Dennis Sgroi, M.D., a pathologist at Massachusetts General Hospital in a statement. "It will be a valuable tool to help identify those patients whose disease will most likely recur, as well as those who will benefit from extended therapy."

Pathwork Validates Tissue of Origin Test, Receives Approval in N.Y.

Pathwork Diagnostics (Redwood City, Calif.) has published results of a multicenter trial validating its microassay tissue of origin test for formalin-fixed, paraffin-embedded (FFPE) specimens and has expanded its testing base into New York.

The Pathwork Tissue of Origin Test is a microarray-based gene expression test that compares RNA expression patterns of the tumor specimen and the 15 tissues on the test panel. It requires small amounts of FFPE tumor tissue and measures the gene expression levels of more than 2,000 genes. The test, which received Food and Drug Administration (FDA) approval in June 2010, covers the same panel of tumor tissues classified by Pathwork's previously approved test for frozen specimens but uses different algorithms and processing methods.

In the study published in the January issue of the *Journal of Molecular Diagnostics*, Pathwork researchers validated the test performance in 462 specimens with overall agreement with the masked reference diagnosis in 89 percent of cases. By comparison, a recent meta-analysis shows immunohistochemistry (IHC) panels correctly identify the primary cancer site in only 66 percent of metastatic cases.

In addition to the positive test results with the Pathwork test, an average of 12 tissues for each specimen could be ruled out with greater than 99 percent probability. A multisite reproducibility study showed 89 percent concordance between laboratories.

The tissue of origin test helps identify the origin of poorly differentiated, undifferentiated, and metastatic tumors, which make up an estimated 3 percent to 5 percent of all new cancer cases. Pinpointing the tissue of origin is increasingly important as targeted therapies, predicated on known primary cancer, are shown to improve clinical outcome. Location of the primary cancer site is also utilized for reimbursement purposes and entry criteria for clinical trials.

In December Pathwork received a clinical laboratory permit to offer the company's testing service in New York. It is the only FDA-cleared tissue of origin testing service available in the state.

MDx Companies Lead IVD Stocks to 11% Gain for 2010

The 18 stocks in the G-2 Diagnostic Stock Index climbed an unweighted average of 11 percent in 2010 versus respective gains of 17 percent and 13 percent for the Nasdaq and the S&P 500.

Sequenom (San Diego) was the best-performing stock in 2010, soaring 94 percent to close at $8.03 per share on Dec. 31, 2010. Last fall, the company completed the build-out of its wholly owned San Diego reference laboratory, the Sequenom Center for Molecular Medicine, and received federal and state CLIA certificates for the facility. Researchers there recently began evaluating the clinical performance of the company's SensiGene T21 assay. The laboratory-developed test (LDT) is designed to detect an overabundance in maternal blood of chromosome 21, which is associated with fetal Down syndrome. Further along in the pipeline is an LDT for age-related macular degeneration, which Sequenom plans to launch during the first half of 2011.

Another molecular diagnostics company that performed strongly in 2010 was **Cepheid** (Sunnyvale, Calif.), which climbed 82 percent to end the year at $22.75 per share. The company has continued to expand adoption of its automated real-time polymerase chain reaction-based platform, GeneXpert, while looking to move into women's health, viral infectious diseases, and oncology applications. In December, Cepheid launched its Xpert flu test in Europe. The CE-marked test simultaneously detects and differentiates flu A, flu B, and 2009 H1N1 influenza virus in about one hour.

IVD Stock Review for 2010

COMPANY (TICKER)	Price 12/31/09	Price 12/31/10	52-WEEK % CHANGE	MARKET CAPITALIZATION
Sequenom (SQNM)	4.14	8.03	94	577M
Cepheid (CPHD)	12.48	22.75	82	1,430M
Gen-Probe (GPRO)	42.92	58.35	36	2,860M
Luminex (LMNX)	14.93	18.28	22	746M
Beckman Coulter (BEC)	65.44	75.23	15	5,040M
OraSure (OSUR)	5.08	5.75	13	309M
Bio-Rad (BIO)	96.46	103.85	8	3,000M
Meridian (VIVO)	21.55	23.16	7	938M
Becton Dickinson (BDX)	78.86	84.52	7	19,320M
Abaxis (ABAX)	25.55	26.85	5	577M
Quidel (QDEL)	13.78	14.45	5	407M
Immucor (BLUD)	20.24	19.83	-2	1,480M
Johnson & Johnson (JNJ)	64.41	61.85	-4	172,450M
Abbott (ABT)	53.99	47.91	-11	73,720M
Alere (ALR)*	41.51	36.60	-12	3,250M
Clinical Data (CLDA)	18.26	15.91	-13	459M
Affymetrix (AFFX)	5.84	5.03	-14	374M
Nanosphere (NSPH)	6.44	4.36	-32	124M
Unweighted Average			11	

**Formerly known as Inverness Medical Innovations*

G-2 Insider

FDA, Life Sciences' Relationship Complicated . . . A new report from PricewaterhouseCoopers LLC (PwC) concludes that while improving, the life sciences industry's relationship with the Food and Drug Administration (FDA) is still plagued by dissatisfaction over the approval process. The report, based on a survey of executives of diagnostics, device, drug, and biologics companies, shows that while companies acknowledge the FDA has improved its guidance in the last two years, resource constraints hamper the approval process and companies do not take full advantage of FDA's existing resources.

The report, Improving American's Health V, is available online at www.pwc.com/us/fdasurvey.

Nearly eight in 10 respondents say that FDA guidance has improved in the past two years, but 60 percent say that the FDA has changed its position on at least one review. Only 8 percent feel that the FDA is doing enough to advance personalized medicine. In addition, the industry doesn't feel the FDA has made a large enough financial commitment to identify biomarkers. More than half of respondents believe the FDA lacks the capabilities to implement the Critical Path Initiative it launched in 2004 to help new drugs reach the market faster through incorporation of new science including biomarker development, bioinformatics, and drug-diagnostic codevelopment.

Respondents also indicated the industry can do better. More than a third of industry leaders acknowledge their companies did not consistently schedule presubmission and end-of-phase meetings with the FDA. The survey showed the industry needs to become more aware of FDA initiatives with more than half of respondents indicating they were not familiar with the Critical Path Initiative, Clinical Trials Transformation Initiative, or the planned Sentinel System to track adverse events.

Company References

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Beckman Coulter 714-993-5321
Cepheid 408-541-4191
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Haverford Health Advisors 610-407-4024
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Save The Date

Molecular Diagnostics Conference
April 13-15, 2011, Boston, Mass.
www.g2reports.com/MDxConference

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