Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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CONTENTS

WASHINGTON G-2 REPORTS

Established 1979

When Will Drug Companies Hop On The Pharmacogenomics Bandwagon?

Taking prescription drugs today is somewhat of a gamble: Different people react differently to the same drugs, leading to adverse side effects or no effect at all. More than 100,000 Americans die each year as a result of adverse drug reactions (ADRs), and the annual bill for treating medication misuse is a stunning $136 billion, according to estimates from the FDA's Center for Drug Evaluation and Research.

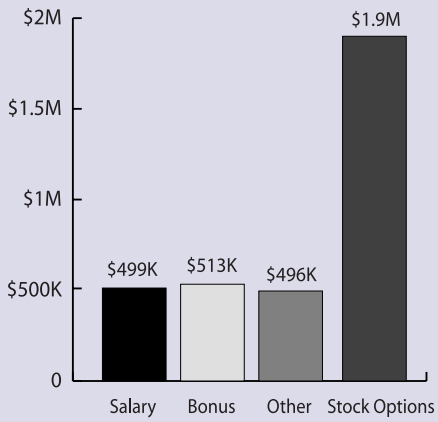
The mapping of the entire human genome, three million bits of DNA that comprise our genetic blueprint, in early 2000 had brought hope for a new era of personalized medicine, or pharmacogenomics, that would help cut down on ADRs. Back then it was thought that drug companies would use information from the Human Genome Project to develop new drugs with companion diagnostics that would allow doctors to match treatments to patients' genes. The result would be safer and more effective medicines, saving lives and money.

But fast forward five years, and not much has changed. The introduction of new drugs linked with gene-based lab tests have been few and far between. So is the "pharmacogenomic revolution" for real? For our answer, see *Inside the Diagnostics Industry*, pp. 5-10.

IVD Execs Got Average $3.4M Each Last Year

The top executives at 25 leading American IVD companies received total compensation (including the value realized from exercised stock options) of $86.1 million last year for an average of about $3.4 million per executive, according to an analysis by *DTTR* of proxy reports filed with the U.S. Securities & Exchange Commission. The average salary for these executives in 2004 was $499,027, up 1% from 2003; bonuses averaged $512,562, up 46%; and "other" compensation (e.g., restricted stock awards, life insurance coverage, forgiven loans, etc.) ➥ *p. 3*

Average IVD Executive Pay



Source: *DTTR* from company proxies

Olson To Lead Roche Diagnostics In North America

Tiffany Olson

Roche Diagnostics has named Tiffany Olson, 45, as its new head of North America, and president and chief executive of Roche Diagnostics Corp. (Indianapolis, IN). These positions were left open when Martin Madaus resigned to become chief executive of Millipore Corp. (see *DTTR*, December 2004, p. 4). Olson has been with Roche since 1997 and is currently responsible for global market development for Roche Diagnostics in Basel, Switzerland. She will officially begin in her new position on June 1. She will report to Heino von Prondzynski, chief executive of Roche Diagnostics worldwide operations. Olson is the first woman to head the division, said spokeswoman Doyia Turner.

Liotta And Petricoin Resigning From Government Research Jobs

National Cancer Institute pathologist Lance Liotta, M.D., Ph.D., and FDA scientist Emanuel Petricoin, Ph.D., have each announced plans to leave their government jobs to take more lucrative research positions with George Mason University.

Liotta and Petricoin were at the center of controversy when former congressman James Greenwood investigated conflicts of interest at the National Institutes of Health (NIH) about one year ago. The Greenwood investigation and subsequent hearings revealed that Liotta and Petricoin had worked as paid consultants for a company, Predicant Biosciences, that is in competition with Correlogic, which the two scientists and the NCI were already collaborating with (*DTTR*, July 2004, page 1). Correlogic and Predicant Biosciences are competitors in the emerging field of blood protein-pattern recognition testing systems for detecting cancer.

Following the Greenwood investigation, the NIH announced new rules that prohibit its employees from entering outside consulting agreements with pharmaceutical companies, hospitals, health insurers, and healthcare providers. The guidelines also mandate that about 6,000 top NIH employees cannot hold stock in pharmaceutical or biotechnology companies.

In contrast to the NIH, researchers at George Mason are encouraged to consult with private companies, according to Vikas Chandhoke, George Mason's associate dean for research. Liotta and Petricoin are expected to play a big role in the development of the new George Mason University-Inova Health System Translational Research Centers, which will apply proteomics and genomics research to primarily study cancer, metabolic syndrome, and liver disease.

Dade Files 510K For Dimension Vista 1500

Dade Behring (Deerfield, IL) says it submitted a 510K to the FDA for its Dimension Vista 1500 high-volume integrated chemistry/immunoassay system. The Vista is targeted for commercialization in the second half of 2006. The system consolidates chemistry and immunoassay testing on a single homogeneous testing format with throughput of 1,500 tests per hour (assuming an average mix of chemistry and immunoassay tests), a Dade spokeswoman tells *DTTR*. She says there will be 90 to 100 tests cleared on the Vista prior to launch, which will include 36 basic chemistry assays along with more than 54 specialty and immunoassay tests.

▲ **IVD Execs Got $3.4 Million,** *from page 1*

was $496,215, up 58%. The biggest component of compensation was stock options, which averaged $1.9 million in value realized per executive.

Jim Reid-Anderson, age 46, chairman and chief executive of **Dade Behring** (Deerfield, IL), was the highest-paid IVD executive in the United States for the second year in a row (see *DTTR*, June 2004, p. 1). Reid-Anderson received total compensation of $15.5 million, including a salary of $865,240, bonus of $2.03 million, and other compensation (i.e., fringe benefits) of $174,463. Last but not least, he gained $12.48 million from exercised stock options. In 2004, Dade posted net income of $79.9 million versus $48.1 million in 2003; Dade's stock price rose 57% in 2004.

The second-highest-paid IVD executive was **Edward Ludwig**, 53, chairman and chief executive of **Becton Dickinson** (Franklin Lakes, NJ), who earned a total of $12.15 million, including salary of $933,689, bonus of $1.2 million, other compensation of $2.22 million, plus $7.8 million from exercised stock options. Becton posted net income of $467.4 million in 2004, down from $547.1 million; its stock price rose 38%.

The third-highest-paid was **Henry Nordhoff**, 63, chairman and chief executive of **Gen Probe** (San Diego, CA). Nordhoff received total compensation of $8.55 million, including salary of $529,669, bonus of $400,000, and other compensation of $932,799. He also got $6.69 million from exercised stock options. Gen Probe increased its net income to $54.58 million in 2004 from $35.33 million in 2003; its stock price was up 84%.

Executive Compensation in Europe

The compensation of the top executives in Europe has always been somewhat of a mystery. Compensation for U.S. executives has been wildly out of control for a long time, but the details on CEO salaries, bonuses, and stock options have always been made transparent to shareholders.

However, disclosure laws are now under review in a number of European countries where a large proportion of executive salaries have not routinely been made public. The latest annual reports from Roche and Bayer are certainly more forthcoming. They show that European executives are keeping pace with their counterparts in the United States when it comes to over-the-top pay packages.

For example, **Franz Humer**, 58, chairman and chief executive of **Roche Group**, earned a total of 16.45 million Swiss francs ($13.8 million) in 2004, including a salary of 6.03 million francs ($5.06 million), bonus of one million francs ($839,419), stock options valued at 1.78 million francs ($1.49 million), plus indirect benefits of 3.15 million francs ($2.65 million) from employer contributions to his retirement plan.

Heino von Prondzynski, 55, CEO of **Roche Diagnostics**, was paid a total of 4.47 million francs ($3.75 million), including a salary of 1.15 million francs ($964,603), bonus of 700,000 francs ($587,150), stock options valued at 578,709 francs ($485,372), and retirement plan contributions of 1.4 million francs ($1.17 million).

Werner Wenning, 58, chairman and chief executive of **Bayer Group**, received total compensation of 2.74 million euros ($3.53 million), including a salary of 711,359 euros ($918,934), fixed and variable bonuses of 1.65 million euros ($2.13 million), and stock options valued at 372,685 euros ($481,434).

2004 IVD Executive Compensation

Company/Executive	Salary	Bonus	Other Comp*	Value of Exercised Options	2004 Total Comp	2004 Company Net Income	2004 Stock % Chg
Abaxis							
Clinton Severson, 56, Chmn.	$285,000	$461,000	$0	$0	$746,000	$23,614,000	-20%
Abbott Labs							
Rick Gonzalez, 51, Pres., med. products	875,385	1,100,000	1,843,503	0	3,818,888	3,235,900,000	0
Affymetrix							
Stephen Fodor, Ph.D., 51, Chmn.	542,789	560,000	13,794	5,783,863	6,900,446	47,608,000	49
Beckman Coulter							
John Wareham, 63, Chmn.	802,423	483,600	132,345	4,359,084	5,777,452	210,900,000	32
Becton Dickinson							
Edward Ludwig, 53, Chmn.	933,689	1,200,000	2,220,302	7,799,725	12,153,716	467,402,000	38
Bio-Rad							
Norman Schwartz, 55, Pres.	477,000	174,403	10,664	327,000	989,067	68,242,000	-1
Biosite							
Kim Blickenstaff, 52, Chmn.	389,058	280,734	1,922	446,481	1,118,195	41,448,000	113
Cholestech							
Warren Pinckert, 60, Pres.	369,465	33,750	8,443	49,222	460,880	8,707,000	7
Cytyc							
Patrick Sullivan, 53, Chmn.	494,769	800,000	6,150	1,994,680	3,295,599	73,588,000	99
Dade Behring							
Jim Reid-Anderson, 46, Chmn.	865,240	2,033,266	174,463	12,476,247	15,549,216	79,900,000	57
Diagnostic Products							
Michael Ziering, 49, Chmn.	555,000	60,000	21,000	602,000	1,238,000	61,735,000	20
Digene							
Evan Jones, 46, Chmn.	365,062	243,000	0	6,720,111	7,328,173	21,542,000	-35
Exact Sciences							
Don Hardison, 54, Pres.	338,872	110,000	0	0	448,872	-18,523,000	-62
Gen Probe							
Henry Nordhoff, 63, Chmn.	529,669	400,000	932,799	6,687,030	8,549,498	54,575,000	84
Immucor							
Edward Gallup, 65, Chmn.	329,500	0	36,550	0	366,050	12,538,000	159
Immunicon							
Edward Erickson, 58, Chmn.	291,574	118,000	8,586	162,435	580,595	-27,933,000	-13
Inverness Medical							
Ron Zwanziger, 51, Chmn.	350,000	550,000	0	0	900,000	-14,987,000	15
Johnson & Johnson							
William Weldon, 56, Chmn.	1,459,231	2,500,000	1,692,051	516,697	6,167,979	8,509,000,000	23
Luminex							
Patrick Balthrop, 48, Pres.	282,169	360,000	2,058,669	0	2,700,838	-3,605,000	-5
Meridian							
William Motto, 63, Chmn.	409,615	388,125	56,723	0	854,463	9,185,000	68
OraSure Technologies							
Douglas Michels, 48, Pres.	206,154	200,000	3,162,750	0	3,568,904	-559,642	-16
Quidel							
Caren Mason, 51, Pres.	142,250	150,000	3,668	0	295,918	-6,287,000	-53
Third Wave Technologies							
John Puisis, 45 Pres.	440,305	286,000	20,987	0	747,292	-8,116,000	93
TriPath Imaging							
Paul Sohmer, M.D., 56, Chmn.	398,000	35,820	0	0	433,820	605,000	15
Ventana							
Christopher 55, Gleeson, Pres.	343,462	286,356	0	461,150	1,090,968	21,289,000	62
Total, 25 execs	12,475,681	12,814,054	12,405,369	48,385,725	86,080,829		
Average, 25 execs	$499,027	$512,562	$496,215	$1,935,429	$3,443,233		29%

*Other compensation includes the value of restricted stock awards, plus company contributions to retirement plans and life insurance policies, forgiven loans, and private use of company cars and airplanes.

Source: *DTTR* from company proxies

Are Drug Companies Stalling The Pharmacogenomic Revolution?

Why haven't the major drug companies embraced pharmacogenomics? *DTTR* thinks it's because pharmacogenomic drug labeling could restrict the use of medicines to patients with a certain genotype or protein expression, leading to significantly smaller markets for new products. These smaller markets could wind up being too small for drug companies to recoup the substantial research and development costs needed to bring a new drug to market.

Currently, the major drug companies operate under the "blockbuster" model, which assumes that a single compound can effectively treat most patients who have a particular condition. Blockbuster drugs may be effective in only 40% to 60% of the general population, but as long as there is no adverse effect in the remaining patients, physicians can prescribe them on a trial-and-error basis.

The need for blockbusters is driven by the enormous amount of time and expense required to develop a new drug. The Tufts Center for the Study of Drug Development (Boston) estimates that it takes an average of eight to 12 years at a cost of more than $800 million to bring a new drug to market. As a result, the major drug companies need to hit homeruns (drugs that generate $1+ billion in annual sales).

However, several recent incidents have raised questions about the safety and effectiveness of the blockbuster approach. Most recently, the Cox-2 inhibitors for treatment of arthritic pain (Vioxx, Bextra, etc.) were pulled from the market because they raised the risks of stroke and heart attacks in some patients. Myla Lai-Goldman, M.D., chief scientific officer and medical director at LabCorp, says the controversy has underscored the need for pharmacogenomic tests that can identify patient populations that will not suffer adverse reactions.

David Johnston, Ph.D., chief scientific officer for clinical trials at LabCorp,

Big Pharma's Reliance on Blockbusters

Last year, U.S. prescription drug sales grew 8.3% to $235.4 billion. Blockbuster drugs (>$1 billion in annual sales) accounted for more than 20% of total sales, and the top 10 drugs accounted for $37.8 billion, or 16% of total sales. Drug company executives may be resisting pharmacogenomics because diagnostic screening will reduce the market size for blockbuster drugs by eliminating large portions of the patient population for which specific drugs do not work or cause adverse reactions.

Top 10 Drugs in 2004 by U.S. Sales *($ millions)*

Rank	Product	Indication	Manufacturer	U.S. Sales*	% Growth
1.	Lipitor	cholesterol reducer	Pfizer	$7,691	14%
2.	Zocor	cholesterol reducer	Merck	4,575	4
3.	Prevacid	for persistent heartburn	Takeda/Abbott	3,802	-5
4.	Nexium	for persistent heartburn	AstraZeneca	3,782	23
5.	Procrit	stimulates red blood cell production	Ortho Biotech/J&J	3,192	-3
6.	Zoloft	antidepressant	Pfizer	3,094	8
7.	Epogen	stimulates red blood cell production	Amgen	2,990	-4
8.	Plavix	anti-blood clotting	Bristol-Myers/ Sanofi-Aventis	2,979	33
9.	Advair Diskus	treats asthma	GlaxoSmithKline	2,914	26
10.	Zyprexa	treats schizophrenia	Eli Lilly	2,826	-10
Total				37,845	

*Represents prescription pharmaceutical purchases at wholesale prices by drug stores, food stores and chains, hospitals, clinics, HMOs, home healthcare, and prisons/universities. Source: IMS Health

believes the major drug companies will embrace personalized medicine in their new drug development efforts once they realize that "gaining 100% of a small market could be more rewarding than getting a small percentage of the total market."

But drug company executives are worried that doctors and patients will become reluctant to take certain drugs, if they learn that these drugs are ineffective or cause adverse reactions in certain segments of the population, according to Jorge Leon, Ph.D., president of Leomics (Princeton, NJ), a consulting firm that specializes in molecular diagnostics and personalized medicine. As a result, he doesn't expect the drug companies to publicize their work in pharmacogenomics until absolutely necessary. He also believes the drug companies are wary of pharmacogenomics because the lab testing part of the equations falls outside of their control.

Herceptin is the biggest success story in personalized medicine, but it happened seven years ago.

The Herceptin Story

The history of Herceptin and its companion diagnostic test, HercepTest, is a good example of how drug companies, diagnostic manufacturers, laboratories, and patients can all benefit from pharmacogenomics, observes *DTTR*.

Genentech initially filed an Investigational New Drug (IND) application for Herceptin in 1991 and completed its Phase 3 clinical trials in early 1997. Genentech had hoped to have Herceptin approved as a broad-brush treatment for breast cancer patients. Although clinical trials showed the drug was not effective as a general treatment, it was found that Herceptin prolonged the life of patients whose breast cancer cells carried amplified HER2 genes and therefore made too much HER2 protein. HER2 overexpression occurs in approximately 25% of women with breast cancer.

Based on this evidence, Herceptin received FDA Fast-Track designation as a product for the treatment of metastatic breast cancer in March 1998. Genentech then worked with the Denmark-based diagnostics company Dako to develop HercepTest, an immunohistochemical test that measures HER2 activity.

In September 1998—only 4.5 months after gaining Fast-Track status—the FDA approved Herceptin for the treatment of HER2 positive metastatic breast cancer as determined by the HercepTest, marking the first combination pharmacogenomic product to reach the market.

LabCorp's Lai-Goldman says the Herceptin/HercepTest story underscores the huge advantages pharmacogenomic research can provide to drug companies in terms of salvaging drugs that might not otherwise make it to the market. Last year, Genetech generated $483.2 million, up 14%, from worldwide sales of Herceptin, making it one of the company's top-selling drugs.

"I'd be surprised if drug companies weren't dusting off the shelves to find drugs that had been killed in clinical trials because of dangerous side effects. Pharmacogenomics could help bring some of these drugs to the market after all," Ed Ashwood, M.D., chief medical officer at ARUP Laboratories (Salt Lake City, UT), tells *DTTR*.

Outside Pressure to Move Toward Pharmacogenomics

LabCorp's Johnston believes that the FDA will someday require genomic data to be submitted before market approval. Steps in that direction were taken with

the recent release of the agency's final guidance on "Pharmacogenomic Data Submissions" and a new drug-diagnostic co-development concept paper from the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD). Together, these documents lay out a regulatory path for new drugs that are co-developed with biomarkers, including what data will be needed during the marketing application review process, the format for submissions, and the data that will be used during regulatory decision making.

Greater use of pharmacogenomics could help drug companies pre-qualify smaller groups of patients enrolled in the clinical trials required to show the efficacy of new drugs. And smaller trials have the potential to significantly reduce the research and development costs associated with the development of targeted drugs, thereby lowering the threshold for commercial viability, notes Johnston.

Separately, Leon says there is pressure building from managed care companies and other payers to speed the use of pharmacogenomics. "Payers realize the tremendous savings that can be gained from getting rid of prescriptions that don't work with patients," he says.

A current example of the substantial savings that targeted medicine can achieve is Erbitux (made by Imclone and marketed by Bristol Myers) and a companion diagnostic test made by DakoCytomation. Erbitux is used for patients who are no longer responding to or cannot take the chemotherapy drug irinotecan. It works by blocking a type of protein called epidermal growth factor receptor (EGFR); the action deprives tumors of an element they need to grow.

The FDA approved Erbitux in February 2004, and one week later it approved the DakoCytomation test kit to help doctors determine which patients express EGFR and are therefore eligible for the treatment.

The average wholesale price for Erbitux is roughly $10,000 per month per patient, or about $20,000 for a typical seven-week treatment cycle. Based on annualized first-quarter reported sales, Bristol Myers and Imclone are on their way to generating some $348 million from Erbitux sales in the United States this year.

Obviously, this is not a drug that the healthcare system can afford to prescribe to patients who will gain no benefit or have an adverse reaction. Reference labs charge several hundred dollars to perform EGFR testing, but that's a bargain considering it will weed out those patients not genetically suited for a $20,000 drug prescription.

Last year, all payers in the United States spent a total of $235.4 billion on prescription drugs (see bottom of page 5), or more than five times the $40 billion to $45 billion that

Current Prescription Drugs with Companion Diagnostics

Drug	Indication	Per-Patient Monthly Cost	Manufacturer	U.S. Sales (millions)*
Erbitux	colorectal cancer	$10,000	Imclone	$348
Gleevec	chronic myelogenous leukemia	2,600	Novartis	468
Herceptin	breast cancer	5,000	Genentech	518
Iressa	lung cancer	1,900	AstraZeneca	120
Total				1,454

*Based on annualized first-quarter 2005 reported sales

Source: DTTR

Washington G-2 estimates was spent on lab and pathology testing. Over time, Leon says pharmacogenomics will lead to an increasing value placed on lab testing services.

What Does Pharmacogenomics Mean for Pathologists?

"I see this [pharmacogenomics] becoming a major role of pathology labs. Instead of just grading cancers, pathologists now have the opportunity to have a greater role in helping oncologists customize treatments for patients," says Allen Gown, M.D., president and medical director of PhenoPath Laboratories (Seattle, WA). "If pathologists don't get on the bandwagon, they'll be left standing," he adds. His advice to pathologists: 1) be aware of all the advances taking place in pharmacogenomics; and 2) work more closely with your oncologist clients. Today, pharmacogenomics is having the greatest impact on breast cancer and hematopathology, but eventually it will hit all areas of pathology, concludes Gown.

Growth Prospects for Pharmacogenomics

Leon estimates that U.S. laboratories and pathology groups are currently performing roughly $100 million of pharmacogenomic testing per year, but that the market will grow to $300 million over the next two years. The key to success for new pharmacogenomic tests will be their ability to direct therapy decisions.

In terms of specific tests, Leon sees the greatest market potential for genetic analysis of mutations in the CYP450 gene for determining antidepressant and antipsychotic drug prescriptions. A number of reference labs already perform CYP450 genetic analysis using homebrew methods, but testing volumes are likely to increase after Roche begins commercialization of its FDA-cleared microarray, AmpliChip CYP450, according to Leon.

He estimates that Roche, which will begin commercialization of AmpliChip CYP450 this summer, will charge labs $300 to $400 per test kit, and that labs will probably charge $700 to $800. But he believes it will be the publication of clinical studies that Roche and other IVD vendors are working on that will drive utilization. "Doctors need to be told how to interpret this test," says Leon. Ultimately, he believes CYP450 genetic analysis could reach peak annual lab testing sales of $500 million per year.

Finally, Leon notes that his review of the pipelines at all the major pharmaceutical companies shows they have a combined 100 clinical trials for targeted cancer drugs underway, including 16 Phase III trials. In general, these new targeted cancer therapies are effective in only 10% to 20% of a given patient population, so the need for accompanying diagnostic tests will be clear.

"Being able to predict response to drugs will revolutionize medicine. We're only at the tip of the iceberg now," concludes Karen Weck, M.D., director of molecular genetics at the University of North Carolina (Chapel Hill).

The Future of Cancer Therapy

The pipeline for targeted therapies is significant and expanding; 100 clinical trials of targeted drugs are underway.

Cancer Type	*Phase I*	*Phase II*	*Phase III*	*Total*
Breast	7	21	4	32
Lung	4	17	7	28
Prostate	8	24	4	36
Colorectal	1	2	1	4
Total	20	64	16	100

Source: Leomics Associates, April 2005

★ The Latest News on Pharmacogenomic Developments ★

Roche To Work With Lilly on Personalized Medicine

Roche Diagnostics has announced a collaboration with Eli Lilly to confirm biomarkers that may be used to identify patients most likely to respond to certain cancer therapies. Lilly and Roche Molecular Diagnostics (Pleasanton, CA) will work with Response Genetics (RGI—Los Angeles, CA), a privately held gene-expression analysis company, with whom both companies have an existing research technology relationship.

The first phase of the agreement specifically targets biomarkers linked to Lilly's Altima (permetrexed) and Gemzar (gemcitabine) anti-cancer treatments. The goal is to confirm biomarkers suspected to be linked to patients' survival response rates. Success of the first phase may lead to the development of companion diagnostic products by Roche.

Gemzar is a chemotherapy drug that has been FDA-approved—when given in combination with cisplatin—for the treatment of metastatic non-small cell lung cancer. Gemzar is also approved—when given in combination with paclitaxel—as a first-line treatment of patients with metastatic breast cancer after they have had chemotherapy with a class of drugs called anthracyclines. Finally, Gemzar is approved for the initial treatment of locally advanced or metastatic cancer of the pancreas. U.S. sales of Gemzar were $565.1 million in 2004, and total worldwide sales were $1.2 billion.

Alimta has been approved by the FDA for the treatment of malignant pleural mesothelioma and for second-line treatment of non-small cell lung cancer. U.S. sales of Alimta totaled $121.8 million last year, and total worldwide sales were $142.6 million.

Genzyme to Develop Test for Targeted Treatment of Lung Cancer

Genzyme Corp. (Westborough, MA) says it will develop a new molecular profiling tool for lung cancer patients now that it has gained exclusive rights to a certain mutation in the EGFR gene discovered by doctors at Massachusetts General Hospital and Dana-Farber Cancer Institute.

Genzyme, which owns the reference lab Genzyme Genetics, says the test will help identify patients with non-small cell lung cancer who are most likely to respond positively to two drugs, Tarceva and Iressa, which are used following at least one failed chemotherapy regimen. The test is expected to be available later this year.

Tarceva is the flagship product of OSI Pharmaceuticals (Melville, NY), while Iressa is marketed by AstraZeneca (London, England).

An estimated 163,000 Americans die of lung cancer every year, according to the American Cancer Society. About 80% to 90% of all lung cancer patients have the non-small cell type.

Mayo Develops Pharmacogenomic Test for Inherited Kidney Disorder for Children

Mayo Clinic (Rochester, MN) researchers have used pharmacogenomics to develop a test and treatment for an inherited kidney disorder, type I primary hyperoxaluria, that can cause organ failure in children and young adults. The findings appear in the current issue of the journal *Kidney International*.

The Mayo researchers discovered that a genetic mutation allows certain kidney stone patients — many of them children — to

benefit from vitamin B6 and have used the finding to develop a genetic test to predict which patients are best suited for this treatment. In discovering the link between a specific mutation and vitamin B6 responsiveness, the Mayo researchers can now use a genetic test for guiding treatment to maximize the probability of swift, successful treatment for select cases of type I primary hyperoxaluria. The disease is uncommon, but if left undiagnosed and untreated, at least half of those affected will suffer kidney failure.

"While there are still questions to resolve — such as determining the most effective dose and the safety of vitamin B6 if very high doses are used — our demonstration of the relationship between a specific mutation and vitamin B6 responsiveness does open the door to informed use of this valuable treatment," says Carla Monico, M.D., Mayo Clinic nephrologist and lead researcher on the study.

Florida Researchers Find Genes Affect How Heart Failure Patients Respond to Drugs

Researchers from the University of Florida (Gainesville) have discovered that patients with heart failure can harbor genetic variations that determine whether they will tolerate the common heart drugs known as beta-blockers. The findings were published recently in the journal *Clinical Pharmacology and Therapeutics*.

In the past five years, beta-blockers have become a standard part of the treatment for heart failure. Patients with the disorder have enlarged hearts that lose the normal heart shape and become rounder and somewhat baggy. Beta-blockers help restore the heart to a more typical shape and size and, in doing so, improve heart function. But patients who start taking beta-blockers must begin at very low doses that are slowly increased over a series of months. Some patients tolerate them well; others have difficulty and suffer adverse reactions such as a worsening of their heart-failure symptoms.

The UF researchers examined blood samples from 61 heart-failure patients and focused on a particular gene called the beta-one adrenergic gene, which makes a protein to which beta-blockers bind. They found that differences within that gene helped predict who would respond most quickly to treatment with a beta-blocker and who would require increased medication and more frequent follow-up visits.

The UF researchers say the findings raise the possibility that the clinical response to at least some beta-blocking agents can be substantially enhanced by selection of patients who have the "hyper-responsive" Arg389Arg beta-1 adrenergic receptor gene variant.

Lancet Study Shows FISH Test Predicts Colon Cancer Treatment Response

An increased number of gene copies for EGFR predicts treatment response to anti-EGFR antibody therapy in patients with metastatic colorectal cancer, according to a study conducted by researchers in Italy.

"Currently, there are no diagnostic tools to identify those likely to benefit from treatment with panitumumab or cetuximab, so patients are exposed to the risk of ineffective therapy with undesired side effects," study co-author Salvatore Siena, M.D., from Ospedale Niguarda Ca'Granda in Milan, said in a statement. Thus, there is a need for tests that can guide therapy.

As reported in the April 14th online issue of *The Lancet Oncology*, Siena's team determined EGFR copy number in 10 patients with an objective response to panitumumab or cetuximab and 21 patients with stable or progressive disease. An increased EGFR copy number was seen in eight of nine patients with an objective response who were assessed using fluorescence in situ hybridization (FISH) testing. In contrast, just one of 21 non-responders had an increased EGFR copy number.

IVD Stocks Rise 3%; Digene Jumps 25%

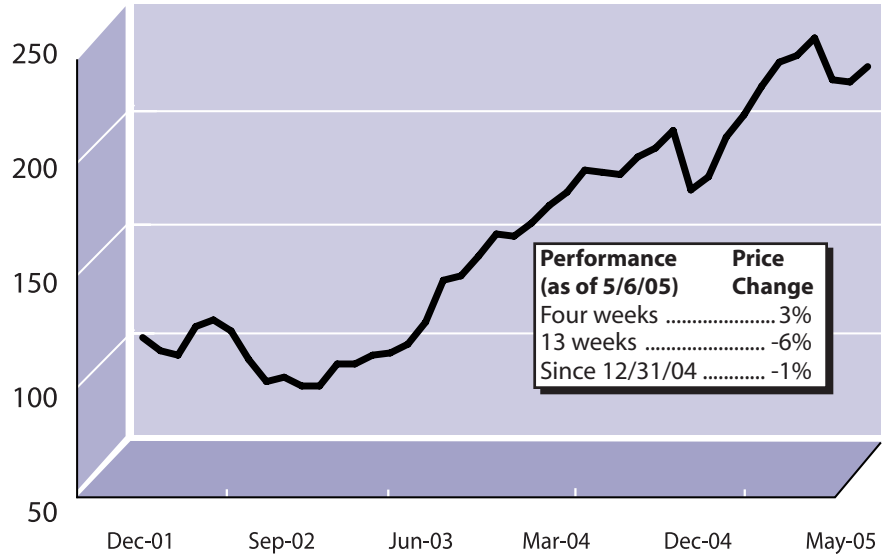
The 21 stocks in the G-2 Diagnostic Stock Index rose an unweighted average of 3% in the four weeks ended May 6, with 14 stocks up in price and seven down. Year to date, the G-2 Index is off 1%, while the S&P 500 Index is down 3% and the Nasdaq is down 10%.

Digene (Gaithersburg, MD) was up 25% to $24.76 per share for a market value of $495 million. The HPV test kit maker posted net income of $1.6 million, or $0.08 per share, in the three months ended March 31, compared with $2.5 million, or $0.12 per share, earned in the year-ago quarter. Revenue was $29.7 million, up from last year's $23.6 million. Analysts following the company had expected earnings of $0.04 per share for the quarter.

In addition, Digene recently announced a licensing agreement with Luminex (Austin, TX) that will give it non-exclusive worldwide rights to commercialize certain diagnostic tests using Luminex's xMAP technology. Digene intends to develop and commercialize certain next-generation products based on xMAP bead-based technology.

Meridian Bioscience (Cincinnatti, OH) rose 16% to $17.43 per share for a market value of $272 million. Meridian's stock was up despite its involvement in a proficiency testing mix up. Between September 2004 and early 2005, Meridian mistakenly included a hazardous flu virus strain in kits shipped to thousands of labs for a College of American Pathologists (CAP) proficiency testing program. CAP learned of the mistake on April 8 and then told the 3,747 labs who received the samples "to destroy them immediately and to report back to the College on that action." On April 27, CAP announced that all of the labs that received the dangerous panels had confirmed they had been destroyed and no one was infected.

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 21 IVD companies.

% price change, Year-to-Date as of 5/6/05

UP	Price	% Chg
Abaxis	$10.15	17%
Abbott Labs	49.02	2
Affymetrix	48.35	7
Becton Dickinson	59.50	2
Bio Rad	52.80	5
Cholestech	10.73	3
Dade Behring	65.22	11
Digene	24.76	25
Immucor	32.90	5
Inverness Medical	26.17	6
Meridian	17.43	16
OraSure	8.33	5
Quidel	4.44	9
Ventana	40.95	12
DOWN		
Beckman Coulter	65.43	-3
Biosite	56.76	-14
Cytyc	22.42	-1
Diagnostic Products	50.71	-1
Gen-Probe	41.82	-16
Johnson & Johnson	68.21	-1
Third Wave	4.11	-18

G-2 Insider

Why do CEOs earn so much? *DTTR* answered this question two years ago (*DTTR*, June 2003, p. 12). "It's because there's a basic conflict of interest between board members and the CEOs they are supposed to be watching on behalf of shareholders. In many cases board members earn a substantial income that can affect their judgment," was our answer back then.

Unfortunately, nothing has changed. Board members in corporate America are still getting paid tens of thousands of dollars for being "yes men" to the CEOs they are supposed to be watching over. Moreover, most CEOs act in the dual role of chief executive and chairman of the board. That's an obvious conflict given that it's the boards that are supposed to negotiate CEO compensation. Note: 16 of the 25 IVD executives listed on page 4 of this issue also act as chairmen.

So what do you get nowadays for serving on a board of directors in corporate America? Well, board members at Johnson & Johnson get $85,000 in cash plus $100,000 worth of stock every year. At Dade Behring, in addition to $55,000 in cash per year, you get $250,000 of stock just for joining the board, and after three years you start getting $65,000 worth of stock every year.

This is a sweet deal considering that the average board member attends only about six to 12 meetings each year, which more often than not turn into weekend golfing, fishing, or dinner parties rather than hard-nosed debate about business strategy.

By voting against compensation plans that CEOs propose for themselves (no matter how outrageous), board members risk losing their board seats and the related pay. By remaining passive, they keep their cushy positions.

Company References

Dade Behring 847-267-5300

Digene 301-944-7000

Genzyme Genetics 800-848-4436

LabCorp 336-584-5171

Leomics Associates 201-248-8313

Mayo Clinic 507-284-2511

Meridian Bioscience 513-271-3700

Roche Diagnostics 317-521-2000

University of Florida (Gainesville) 352-392-3261

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